1: Life Sci. 1994;55(13):1061-9.

Natural flavonoids and lignans are potent cytostatic agents agai human leukemic HL-60 cells.

Hirano T, Gotoh M, Oka K.

Department of Clinical Pharmacology, Tokyo College of Pharmacy, Japan.

Anti leukemic-cell efficacy of 28 naturally occurring and synthetic flavonoid and 11 naturally occurring lignans on human promyelocytic leukemic cell lin HL-60 were examined using MTT assay methods. Differences between anti c proliferative activity and cytotoxicity of these compounds were compared wi those of 4 clinical anti-cancer agents. Eight of the 28 flavonoids and 4 of the lignans showed considerable suppressive effects on HL-60 cell growth with IC50s ranging from 10-940 ng/ml. Among these compounds, genistein, honokiol, machilin A, matairesinol, and arctigenin had the strongest effects v IC50s less than 100 ng/ml, which were almost equivalent to the effects of current anti-cancer agents. The flavonoid genistein and the lignans, however, showed little or no cytotoxicity against HL-60 cells as assessed by dye exclu tests (LC50s > 2,900 ng/ml), whereas the regular anti-cancer agents had pote cytotoxicity. All of the flavonoids and lignans, except for machilin A and arctigenin, were less effective against growth of human T lymphocytic leuke cell line MOLT-4. In addition, the flavonoid and the lignans showed little or inhibiting activity on mitogen-induced blastogenesis of human peripheral-blc lymphocytes. The lignans and genistein were strongly suppressive against incorporations of [3H]thymidine, [3H]uridine, and [3H]leucine into HL-60 c These results showed that some of the naturally occurring flavonoids and lig inhibited HL-60 cell growth with a non-toxic mechanism, possibly via cessat of DNA, RNA, and/or protein synthesis of the leukemic cells.

PMID: 8084211 [PubMed - indexed for MEDLINE]

☐ 1: Res Exp Med (Berl). 1999 Apr;198(6):299-306.

Nitecapone inhibits myeloperoxidase in vitro and enhances functional performance after 8 h of ischemia in experimental he transplantation.

Vento AE, Ramo OJ, Nemlander AT, Ahotupa M, Nissinen E, Holopaine A, Mattila SP.

Department of Thoracic and Cardiovascular Surgery, Helsinki University Central Hospital, Finland.

Nitecapone (NC) has been shown to have beneficial effects on the functional recovery of rat hearts in Langendorff-preparation. The present study was executed to evaluate the effect of NC on preservation of grafts in heart transplantation and the role of NC in the inhibition of granulocyte infiltration Donor hearts were perfused and stored at +4 degrees C for 8 h in either Ringe solution in the control-group (C-group, n = 26) or in NC (50 microM) added Ringer solution (NC-group, n = 18). The heterotopic heart transplantation wa performed. The rats in both groups were killed at either 10 min or 60 min aft release of the aortic clamp and tissue samples were obtained for antioxidative capacity, myeloperoxidase activity, and lipid peroxidation measurements. In vitro studies were performed using sodium azide or nitecapone to inhibit myeloperoxidase (MPO) activity of isolated human leukocytes. A total of 61 of the grafts began to beat in the NC-group, compared to 46% in the control group. Using an arbitrary scale of functional performance, only 33% (4/12) o the grafts were classified as well functioning in the control group, compared 82% (9/11) in the NC-group ($P<0.05$). MPO activity was equal in both group after 10 min but significantly lower after 60 min in the NC-group as compare the control group ($P<0.05$). In vitro studies demonstrated that NC inhibits 50 of purified MPO activity at a concentration of 10 microM. NC did not significantly affect lipid peroxidation or the preservation of endogenous antioxidants. Since NC inhibited myeloperoxidase both in vitro and in vivo, i seems that the positive effects of NC on graft preservation may be mediated the inhibition of granulocyte infiltration.

PMID: 10369086 [PubMed - indexed for MEDLINE]

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=> s hydroxymatairesinol
L1 170 HYDROXYMATAIRESINOL

=> s l1 and phagocytes
L2 1 L1 AND PHAGOCYTES

=> d l2 cbib abs

L2 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
2003:414080 Document No. 138:379228 Method using lignans for inhibiting overactivity of **phagocytes** or lymphocytes in an individual, and therapeutic use. Ahotupa, Markku; Eriksson, John; Kangas, Lauri; Unkila, Mikko; Komi, Janne; Perala, Merja; Korte, Helena (Finland). U.S. Pat. Appl. Publ. US 2003100514 A1 20030529, 10 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-991971 20011126.

AB The invention provides a method for inhibiting the overactivity of **phagocytes** or lymphocytes in an individual by administering to the individual an effective amount of a lignan, wherein (i) the **phagocytes** are neutrophils and the lignan is **hydroxymatairesinol** or matairesinol or mixts. thereof; or (ii) the **phagocytes** are cells of myeloid origin and the lignan is enterolactone or **hydroxymatairesinol** or mixts. thereof; or (iii) the lymphocytes are T-lymphocytes and the lignan is **hydroxymatairesinol**, matairesinol or enterolactone or mixts. thereof. The invention also provides a method for treating or preventing an acute ischemia-reperfusion injury or a chronic condition, caused by overactivity of **phagocytes** or lymphocytes in an individual, the method comprising decreasing the activity of **phagocytes** in an individual by administering to the individual an effective amount of a lignan.

=> s l1 and lymphocyte
L3 1 L1 AND LYMPHOCYTE

=> d l3 cbib abs

L3 ANSWER 1 OF 1 CAPLUS COPYRIGHT 2004 ACS on STN
2003:414080 Document No. 138:379228 Method using lignans for inhibiting overactivity of phagocytes or **lymphocytes** in an individual, and therapeutic use. Ahotupa, Markku; Eriksson, John; Kangas, Lauri; Unkila, Mikko; Komi, Janne; Perala, Merja; Korte, Helena (Finland). U.S. Pat. Appl. Publ. US 2003100514 A1 20030529, 10 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-991971 20011126.

AB The invention provides a method for inhibiting the overactivity of phagocytes or **lymphocytes** in an individual by administering to the individual an effective amount of a lignan, wherein (i) the phagocytes are neutrophils and the lignan is **hydroxymatairesinol** or matairesinol or mixts. thereof; or (ii) the phagocytes are cells of

myeloid origin and the lignan is enterolactone or **hydroxymatairesinol** or mixts. thereof; or (iii) the **lymphocytes** are T-**lymphocytes** and the lignan is **hydroxymatairesinol**, matairesinol or enterolactone or mixts. thereof. The invention also provides a method for treating or preventing an acute ischemia-reperfusion injury or a chronic condition, caused by overactivity of phagocytes or **lymphocytes** in an individual, the method comprising decreasing the activity of phagocytes in an individual by administering to the individual an effective amount of a lignan.

=> s l1 and enterolactone
L4 55 L1 AND ENTEROLACTONE

=> dup remove l4
PROCESSING COMPLETED FOR L4
L5 22 DUP REMOVE L4 (33 DUPLICATES REMOVED)

=> d l5 1-22 cbib abs

L5 ANSWER 1 OF 22 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
2004:181735 Document No.: PREV200400185021. Food additive or product or a pharmaceutical preparation, comprising **hydroxymatairesinol.** Ahotupa, Markku [Inventor, Reprint Author]; Eckerman, Christer [Inventor]; Kangas, Lauri [Inventor]; Makela, Sari [Inventor]; Saarinen, Niina [Inventor]; Santti, Risto [Inventor]; Warri, Anni [Inventor]. Turku, Finland. ASSIGNEE: Hormos Nutraceutical Oy Ltd., Turku, Finland. Patent Info.: US 6689809 February 10, 2004. Official Gazette of the United States Patent and Trademark Office Patents, (Feb 10 2004) Vol. 1279, No. 2. http://www.uspto.gov/web/menu/patdata.html. e-file. ISSN: 0098-1133 (ISSN print). Language: English.
AB This invention relates to methods for prevention of cancers, certain non-cancer, hormone dependent diseases and/or cardiovascular diseases in a person, based on administering of **hydroxymatairesinol** to said person. The invention also concerns a method for increasing the level of **enterolactone** or another metabolite of **hydroxymatairesinol** in a person's serum thereby causing prevention of a cancer or a certain non-cancer, hormone dependent disease in a person, based on administering of **hydroxymatairesinol** to said person. Furthermore, this invention relates to pharmaceutical preparations, food additives and food products comprising **hydroxymatairesinol.**

L5 ANSWER 2 OF 22 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
2004:422662 The Genuine Article (R) Number: 815JG. Radical carboxyarylation approach to lignans. Total synthesis of (-)-arctigenin, (-)-matairesinol, and related natural products. Fischer J (Reprint); Reynolds A J; Sharp L A; Sherburn M S. Univ Sydney, Sch Chem, Sydney, NSW 2006, Australia (Reprint); Australian Natl Univ, Res Sch Chem, Canberra, ACT 0200, Australia. ORGANIC LETTERS (29 APR 2004) Vol. 6, No. 9, pp. 1345-1348. Publisher: AMER CHEMICAL SOC. 1155 16TH ST, NW, WASHINGTON, DC 20036 USA. ISSN: 1523-7060. Pub. country: Australia. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Total syntheses of seven biologically important lignan natural products, including (-)-arctigenin, (-)-matairesinol, and (-)-alpha-conidendrin, by way of a highly stereoselective domino radical sequence is presented. The reported stereochemistry of the natural product 7-hydroxyarctigenin is shown to be erroneous; a diastereoisomeric structure is assigned to the natural product.

L5 ANSWER 3 OF 22 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 1
2004:598380 The Genuine Article (R) Number: 832OP. A new lariciresinol-type butyrolactone lignan derived from **hydroxymatairesinol** and its

identification in spruce wood. Eklund P C (Reprint); Willfor S M; Smeds A I; Sundell F J; Sjoholm R E; Holmbom B R. Abo Akad Univ, Proc Chem Ctr, Dept Organ Chem, Biskopsgatan 8, FIN-20500 Turku, Finland (Reprint); Abo Akad Univ, Proc Chem Ctr, Dept Organ Chem, FIN-20500 Turku, Finland; Abo Akad Univ, Proc Chem Ctr, Lab Wood & Paper Chem, FIN-20500 Turku, Finland. JOURNAL OF NATURAL PRODUCTS (JUN 2004) Vol. 67, No. 6, pp. 927-931. Publisher: AMER CHEMICAL SOC. 1155 16TH ST, NW, WASHINGTON, DC 20036 USA. ISSN: 0163-3864. Pub. country: Finland. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB When the natural lignan **hydroxymatairesinol** (1) was treated with an alkaline aqueous solution, it partially rearranged to isomeric forms of a lariciresinol-type butyrolactone lignan. The two major diastereomers formed (2 and 3) were isolated by column and medium-pressure chromatography, and their structures were elucidated by MS and NMR techniques. These previously unknown butyrolactone lignans were identified as naturally occurring in spruce knotwood by GC, GC-MS, and HPLC-ESI MS/MS analyses. The formation of isohydroxymatairesinol (2) and epi-isohydroxymatairesinol (3) from **hydroxymatairesinol** (1), and their detection in rat urine after administration of 1, is discussed.

L5 ANSWER 4 OF 22 MEDLINE on STN DUPLICATE 2

2004200177. PubMed ID: 15096654. Chemopreventive effects of **hydroxymatairesinol** on uterine carcinogenesis in Donryu rats. Katsuda Shin-ichi; Yoshida Midori; Saarinen Niina; Smeds Annika; Nakae Dai; Santti Risto; Maekawa Akihiko. (Department of Biological Safety Research, Japan Food Research Laboratories, Tama-shi, Tokyo 206-0025, Japan.. katudas@jfrl.or.jp) . Experimental biology and medicine (Maywood, N.J.), (2004 May) 229 (5) 417-24. Journal code: 100973463. ISSN: 1535-3702. Pub. country: United States. Language: English.

AB **Hydroxymatairesinol** (HMR), obtained from the heartwood of spruce (Picea abies), has been demonstrated to exert chemo-preventive effects on the development of mammary tumors in rats. To examine the influence of HMR on uterine carcinogenesis, adult Donryu rats were initiated with a single intrauterine treatment of N-ethyl-N'-nitro-N-nitrosoguanidine (ENNG) at 11 weeks of age and fed thereafter 0, 200, or 600 ppm HMR mixed in the soy-containing diet until 15 months of age. Incidences of uterine adenocarcinoma in both 200 and 600 ppm HMR-dosed groups were significantly reduced to 11% and 15%, respectively, less than 50% of 0 ppm, at the end of the experiment ($P < 0.05$). A delay in the start of persistent estrus by HMR was observed at 8 months of age compared with controls given carcinogen alone. From urinalysis, HMR was metabolized mainly to **enterolactone** and hydroxyenterolactone. These findings suggest that HMR or its metabolites exert chemo-preventive effects in the rat ENNG-uterine carcinogenesis model.

L5 ANSWER 5 OF 22 MEDLINE on STN DUPLICATE 3

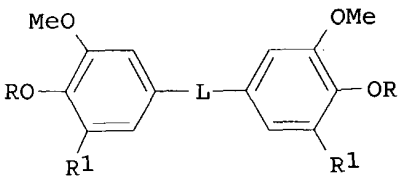
2004363179. PubMed ID: 15265601. Prenatal developmental toxicity study with 7-**hydroxymatairesinol** potassium acetate (HMRlignan) in rats. Wolterbeek A P M; Roberts A; Korte H; Unkila M; Waalkens-Berendsen D H. (TNO Nutrition and Food Research, Toxicology and Applied Pharmacology Department, Zeist, The Netherlands.. wolterbeek@voeding.tno.nl) . Regulatory toxicology and pharmacology : RTP, (2004 Aug) 40 (1) 1-8. Journal code: 8214983. ISSN: 0273-2300. Pub. country: United States. Language: English.

AB Plant lignan 7-hydromatairesinol, a novel precursor of the mammalian lignan **enterolactone** was evaluated in a prenatal developmental toxicity study conducted in the Wistar rat. Mated female rats were fed diets containing 0, 0.25, 1, and 4% (w/w) of 7-**hydroxymatairesinol** in the form of potassium acetate complex (HMRlignan; potassium acetate level approximately 20% w/w within the preparation) for days 0-21 of gestation. Test substance intake was calculated to be 0.14-0.18, 0.46-0.74, and 1.19-2.93 g/kg body weight/day for the low, mid, and high-dose groups, respectively. The rats were sacrificed on day 21 of the gestation period and examined for standard parameters of reproductive performance (fecundity index, gestation index, number of corpora lutea,

number of implantations, pre- and post-implantation loss, number of early- and late resorptions, number of live- and dead fetuses, sex-ration and the weight of the reproductive organs). The fetuses were examined for external, visceral, and skeletal alterations. The results from this study showed no effects on reproductive performance or any treatment related findings following external, visceral, and skeletal examination of the fetuses. However, approximately half of the mated dams of the high-dose failed to thrive due to an unexpected large decrease in their food intake, and were sacrificed early. Body weights of the remaining animals of the high-dose group were decreased. Food consumption was decreased in all treatment groups during the first three days of the gestation period as a result of decreased palatability of the feed. In conclusion, the no-observed-effect level (NOEL) for maternal effects was 1%, whereas the NOEL for fetal development following daily oral HMRlignan administration throughout the gestation was equivalent to 4% in the diet.

L5 ANSWER 6 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN
2003:633624 Document No. 139:179926 Preparation of lignan ester derivatives for use in pharmaceutical compositions and dietary supplements. Eklund, Patrik; Hiilovaara-Teijo, Mervi; Kalapudas, Arja; Kangas, Lauri; Lindholm, Anna; Sjoeholm, Rainer; Soedervall, Marja; Unkila, Mikko (Hormos Nutraceutical Oy Ltd., Finland). PCT Int. Appl. WO 2003066556 A1 20030814, 35 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-FI41 20030121. PRIORITY: FI 2002-222 20020205; FI 2002-563 20020325.

GI



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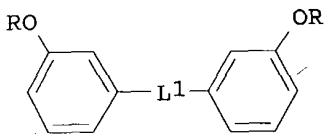

II

AB The invention relates to novel phenolic esters of lignans I (R = COR', SO2R'; R1 = H, OMe; R' = (un)substituted C1-22-alkyl, alkenyl, arylalkyl, aralkenyl, aromatic (substituted with OH, carboxyl, oxo, amino); L = skeleton of **hydroxymatairesinol**, matairesinol, lariciresinol, secoisolariciresinol, isolariciresinol, oxomatairesinol,

α-conidendrin, pinoresinol, liovil, picearesinol, arctigenin, syringaresinol, nortrachelogenin) and II (L1 = enterodiol, R ≠ Ac, COEt; L1 = **enterolactone**), their geometric or stereoisomers. Thus, matairesinol dibutyrate was prepared from matairesinol via acylation with EtCOCl in CH2Cl2 containing pyridine. Furthermore, the invention concerns pharmaceutical compns., dietary supplements, and food products comprising said esters.

L5 ANSWER 7 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

2003:590821 Document No. 139:128028 Method for prevention of diseases in coeliac patients. Unkila, Mikko (Finland). U.S. Pat. Appl. Publ. US 2003144216 A1 20030731, 5 pp. (English). CODEN: USXXCO. APPLICATION: US 2002-54900 20020125.

AB Methods for prevention of cancers, precancers, certain non-cancer, hormone dependent diseases and/or cardiovascular diseases in a person suffering from coeliac disease, based on administering of a lignan to the person. A method for increasing the level of **enterolactone** or another metabolite of a lignan in a person's serum is also disclosed, where the person suffers from coeliac disease, thereby causing prevention of a cancer or a certain non-cancer, hormone dependent disease in the person, based on administering of a lignan to the person.

L5 ANSWER 8 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

2003:414080 Document No. 138:379228 Method using lignans for inhibiting overactivity of phagocytes or lymphocytes in an individual, and therapeutic use. Ahotupa, Markku; Eriksson, John; Kangas, Lauri; Unkila, Mikko; Komi, Janne; Perala, Merja; Korte, Helena (Finland). U.S. Pat. Appl. Publ. US 2003100514 A1 20030529, 10 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-991971 20011126.

AB The invention provides a method for inhibiting the overactivity of phagocytes or lymphocytes in an individual by administering to the individual an effective amount of a lignan, wherein (i) the phagocytes are neutrophils and the lignan is **hydroxymatairesinol** or matairesinol or mixts. thereof; or (ii) the phagocytes are cells of myeloid origin and the lignan is **enterolactone** or **hydroxymatairesinol** or mixts. thereof; or (iii) the lymphocytes are T-lymphocytes and the lignan is **hydroxymatairesinol**, matairesinol or **enterolactone** or mixts. thereof. The invention also provides a method for treating or preventing an acute ischemia-reperfusion injury or a chronic condition, caused by overactivity of phagocytes or lymphocytes in an individual, the method comprising decreasing the activity of phagocytes in an individual by administering to the individual an effective amount of a lignan.

L5 ANSWER 9 OF 22 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN

2003:545188 The Genuine Article (R) Number: 691LX. Oxidative transformation of the natural lignan **hydroxymatairesinol** with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone. Eklund P C (Reprint); Sjoholm R E. Abo Akad Univ, Dept Organ Chem, Proc Chem Grp, Piispankatu 8, Turku 20500, Finland (Reprint); Abo Akad Univ, Dept Organ Chem, Proc Chem Grp, Turku 20500, Finland. TETRAHEDRON (16 JUN 2003) Vol. 59, No. 25, pp. 4515-4523. Publisher: PERGAMON-ELSEVIER SCIENCE LTD. THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND. ISSN: 0040-4020. Pub. country: Finland. Language: English.

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The oxidative transformation of the two isomers of the natural lignan **hydroxymatairesinol** from Norway Spruce (Picea abies) by 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), has been studied. Significant differences in the outcome of the reactions were observed when the pure isomers of **hydroxymatairesinol** were reacted with DDQ under the same conditions. The different stereoelectronic effects in the two isomers as well as their conformational structures seem to determine the site of reaction, which results in different reaction products. Several products were identified by GC-MS and NMR spectroscopy.

Oxomatairesinol was obtained in a yield of 25%. (C) 2003 Elsevier Science Ltd. All rights reserved.

L5 ANSWER 10 OF 22 MEDLINE on STN DUPLICATE 4
2003073811. PubMed ID: 12583751. Synthesis of (-)-matairesinol, (-)-**enterolactone**, and (-)-enterodiol from the natural lignan **hydroxymatairesinol.** Eklund Patrik; Lindholm Anna; Mikkola J-P; Smeds Annika; Lehtila Reko; Sjoholm Rainer. (Department of Organic Chemistry, Abo Akademi University, Biskopsgatan 8, 20500-FIN, Abo, Finland.. paeklund@abo.fi) . Organic letters, (2003 Feb 20) 5 (4) 491-3. Journal code: 100890393. ISSN: 1523-7060. Pub. country: United States. Language: English.
AB [reaction: see text] We describe here a four-step semisynthetic method for the preparation of enantiomerically pure (-)-**enterolactone** starting from the readily available lignan **hydroxymatairesinol** from Norway spruce (Picea abies). **Hydroxymatairesinol** was first hydrogenated to matairesinol. Matairesinol was esterified to afford the matairesinyl 4,4'-bistriflate, which was deoxygenated by palladium-catalyzed reduction to 3,3'-dimethylenterolactone. Demethylation of 3,3'-dimethylenterolactone and reduction with LiAlH(4) yielded (-)-**enterolactone** and (-)-enterodiol, respectively.

L5 ANSWER 11 OF 22 MEDLINE on STN DUPLICATE 5
2003372627. PubMed ID: 12906904. Liquid chromatographic-tandem mass spectrometric method for the plant lignan 7-**hydroxymatairesinol** and its potential metabolites in human plasma. Smeds Annika; Hakala Kristo. (Abo Akademi University, Department of Organic Chemistry, Biskopsgatan 8, FIN-20500, Turku, Finland.. ansmeds@abo.fi) . Journal of chromatography. B, Analytical technologies in the biomedical and life sciences, (2003 Aug 15) 793 (2) 297-308. Journal code: 101139554. ISSN: 1570-0232. Pub. country: United States. Language: English.
AB A HPLC-MS-MS method was developed for the determination of the plant lignan 7-**hydroxymatairesinol** and its potential metabolites matairesinol, oxomatairesinol, alpha-conidendrin, 7-hydroxyenterolactone, enterodiol, and **enterolactone** in human plasma. The method included sample cleanup by solid-phase extraction (SPE) and analysis using a PE Sciex API3000 triple quadrupole mass spectrometer with electrospray ionisation. The lignans were quantified using two deuterated internal standards. They showed good chromatographic linearity, analysis repeatability, and SPE recovery in the presence of plasma. In pooled plasma and in plasma samples collected from two individual subjects lignan glucuronides and sulfates were enzymatically hydrolysed to free lignans and then analysed. All the lignans could be detected in the samples.

L5 ANSWER 12 OF 22 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
2003:991973 The Genuine Article (R) Number: 741GM. Lack of significant inhibitory effects of a plant lignan tracheloside on 2-amino-1-methyl-6-phenylimidazo [4,5-b]pyridine (PhIP)-induced mammary carcinogenesis in female Sprague-Dawley rats. Kitamura Y; Yamagishi M; Okazaki K; Son H Y; Imazawa T; Nishikawa A; Iwata T; Yamauchi Y; Kasai M; Tsutsumi K; Hirose M (Reprint). Natl Inst Hlth Sci, Div Pathol, Setagaya Ku, 1-18-1 Kamiyoga, Tokyo 1588501, Japan (Reprint); Natl Inst Hlth Sci, Div Pathol, Setagaya Ku, Tokyo 1588501, Japan; Chungnam Natl Univ, Coll Vet Med, Taejon 305764, South Korea; Rinoru Oil Mills Co Ltd, Tokyo, Japan. CANCER LETTERS (28 OCT 2003) Vol. 200, No. 2, pp. 133-139. Publisher: ELSEVIER SCI IRELAND LTD. CUSTOMER RELATIONS MANAGER, BAY 15, SHANNON INDUSTRIAL ESTATE CO, CLARE, IRELAND. ISSN: 0304-3835. Pub. country: Japan; South Korea. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Tracheloside, one of the plant lignans which can be extracted from the debris after safflower oil is produced from the seeds of Carthamus tinctorious, is an analogue of another plant lignan, arctiin, the side-chain C-2 of the five-membered ring being changed from a hydrogen to a hydroxyl group. We have already demonstrated that arctiin has

chemopreventive effect on mammary carcinogenesis. Therefore, chemopreventive effects of tracheloside on the initiation or post-initiation period of 2-amino-1 -methyl-6-phenylimidazo[4,5-b]pyridine (PhIP)-induced mammary carcinogenesis in female rats were examined. For initiation, female Sprague-Dawley (SD) rats at the 6 weeks of age were given intragastric administrations of 100 mg/kg body weight of PhIP once a week for 8 weeks. The animals were treated with 0.2 or 0.02% tracheloside during or after this carcinogen exposure. Control rats were fed basal diet with PhIP initiation or 0.2% tracheloside or basal diet alone without initiation throughout the experimental period. All surviving animals were necropsied at the week 52 of administration. There were no clear treatment-related changes with statistical significance in all parameters for mammary carcinomas measured in this experiment. These results indicate that tracheloside may not exert significant effects on PhIP-induced mammary carcinogenesis at least under the present experiment condition.

L5 ANSWER 13 OF 22 EMBASE
on STN
2003267147 EMBASE Bioavailability of phyto-oestrogens. Rowland I.; Faughnan M.; Hoey L.; Wahala K.; Williamson G.; Cassidy A.. Dr. I. Rowland, Northern Ireland Ctr. for Food/Hlth., University of Ulster, Coleraine BT52 1SA, United Kingdom. i.rowland@ulst.ac.uk. British Journal of Nutrition 89/SUPPL. 1 (S45-S58) 1 Jun 2003.
Refs: 81.
ISSN: 0007-1145. CODEN: BJNUAV. Pub. Country: United Kingdom. Language: English. Summary Language: English.
AB The term phyto-oestrogen encompasses isoflavone compounds, such as genistein and daidzein, found predominantly in soya products and the lignans, such as matairesinol and secoisolariciresinol, found in many fruits, cereals and in flaxseed. There is evidence that they have potential health benefits in man particularly against hormone-dependent diseases such as breast and prostate cancers and osteoporosis. This has led to intense interest in their absorption and biotransformation in man. The metabolism of isoflavones and lignans in animals and man is complex and involves both mammalian and gut microbial processes. Isoflavones are present predominantly as glucosides in most commercially available soya products; there is evidence that they are not absorbed in this form and that their bioavailability requires initial hydrolysis of the sugar moiety by intestinal β-glucosidases. After absorption, phyto-oestrogens are reconjugated predominantly to glucuronic acid and to a lesser degree to sulphuric acid. Only a small portion of the free aglycone has been detected in blood, demonstrating that the rate of conjugation is high. There is extensive further metabolism of isoflavones (to equol and O-desmethyl-angolensin) and lignans (to enterodiol and **enterolactone**) by gut bacteria. In human subjects, even those on controlled diets, there is large interindividual Variation in the metabolism of isoflavones and lignans, particularly in the production of the gut bacterial metabolite equol (from daidzein). Factors influencing absorption and metabolism of phyto-oestrogens include diet and gut microflora.

L5 ANSWER 14 OF 22 EMBASE
on STN
2003267142 EMBASE Analysis of phyto-oestrogens in biological matrices. Hoikkala A.A.; Schiavoni E.; Wahala K.. Prof. K. Wahala, Department of Chemistry, Laboratory of Organic Chemistry, University of Helsinki, PO Box 55, FIN-00014 Helsinki, Finland. kristiina.wahala@helsinki.fi. British Journal of Nutrition 89/SUPPL. 1 (S5-S18) 1 Jun 2003.
Refs: 95.
ISSN: 0007-1145. CODEN: BJNUAV. Pub. Country: United Kingdom. Language: English. Summary Language: English.
AB A review covering different methods for the analysis of phyto-oestrogens in biological matrices is presented. Sample pretreatment and analysis of isoflavonoids and lignans by HPLC and GC with various detection methods

are discussed. The immunoassay method is also briefly presented.

L5 ANSWER 15 OF 22 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

2002:583081 Document No.: PREV200200583081. USE OF **HYDROXYMATAIRESINOL** FOR PREVENTION OF CANCERS, NON-CANCER, HORMONE DEPENDENT DISEASES AND CARDIOVASCULAR DISEASES BY **HYDROXYMATAIRESINOL**, AND A PHARMACEUTICAL PREPARATION, FOOD ADDITIVE AND FOOD PRODUCT COMPRISING **HYDROXYMATAIRESINOL.** Ahotupa, Markku [Inventor, Reprint author]; Eckerman, Chester [Inventor]; Kangas, Lauri [Inventor]; Makela, Sari [Inventor]; Saarinen, Niina [Inventor]; Santti, Risto [Inventor]; Warri, Anni [Inventor]. Turku, Finland. ASSIGNEE: Hormos Nutraceutical Oy Ltd., Turku, Finland. Patent Info.: US 6451849 September 17, 2002. Official Gazette of the United States Patent and Trademark Office Patents, (Sep. 17, 2002) Vol. 1262, No. 3. http://www.uspto.gov/web/menu/patdata.html. e-file.
CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

AB This invention relates to methods for prevention of cancers, certain non-cancer, hormone dependent diseases and/or cardiovascular diseases in a person, based on administering of **hydroxymatairesinol** to said person. The invention also concerns a method for increasing the level of **enterolactone** or another metabolite of **hydroxymatairesinol** in a person's serum thereby causing prevention of a cancer or a certain non-cancer, hormone dependent disease in a person, based on administering of **hydroxymatairesinol** to said person. Furthermore, this invention relates to pharmaceutical preparations, food additives and food products comprising **hydroxymatairesinol.**

L5 ANSWER 16 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

2002:392225 Document No. 136:380145 Prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases by use of **hydroxymatairesinol**, and a pharmaceutical preparation, food additive and food product comprising **hydroxymatairesinol.** Ahotupa, Markku; Eckerman, Christer; Kangas, Lauri; Makela, Sari; Saarinen, Niina; Santti, Risto; Warri, Anni (Hormos Nutraceutical oy Ltd., Finland). U.S. Pat. Appl. Publ. US 2002061854 A1 20020523, 15 pp., Cont.-in-part of U.S. Ser. No. 829,944. (English). CODEN: USXXCO. APPLICATION: US 2001-972850 20011010. PRIORITY: US 1999-281094 19990330; US 2001-829944 20010411.

AB The invention discloses methods for prevention of cancers, certain non-cancerous, hormone-dependent diseases, and/or cardiovascular diseases in a person, based on the administration of **hydroxymatairesinol.** The invention also discloses a method for increasing the level of **enterolactone** or another metabolite of **hydroxymatairesinol** in a person's serum, thereby causing prevention of a cancer or a certain non-cancerous, hormone-dependent disease in a person, based on administration of **hydroxymatairesinol.** Furthermore, the invention discloses pharmaceutical prepns., food additives, and food products comprising **hydroxymatairesinol.**

L5 ANSWER 17 OF 22 MEDLINE on STN DUPLICATE 6

2002484700. PubMed ID: 12270222. Structural determinants of plant lignans for the formation of **enterolactone** in vivo. Saarinen Niina M; Smeds Annika; Makela Sari I; Ammala Jenni; Hakala Kristo; Pihlava Juha-Matti; Ryhanen Eeva-Liisa; Sjoholm Rainer; Santti Risto. (Department of Anatomy, Institute of Biomedicine, University of Turku, FIN-20520, Turku, Finland.) Journal of chromatography. B, Analytical technologies in the biomedical and life sciences, (2002 Sep 25) 777 (1-2) 311-9. Journal code: 101139554. ISSN: 1570-0232. Pub. country: United States. Language: English.

AB The quantity of mammalian lignans **enterolactone** (ENL) and enterodiol (END) and of plant lignans secoisolariciresinol (SECO) and 7-**hydroxymatairesinol** (HMR) excreted in a 24-h rat urine sample was measured after a single p.o. dose of an equivalent quantity of secoisolariciresinol diglycoside (SDG), secoisolariciresinol (SECO),

matairesinol (MR), 7-**hydroxymatairesinol** (HMR) and ENL. Plant lignans (SECO and HMR) were partially absorbed as such. The aglycone form of SECO was more efficiently converted into mammalian lignans END and ENL than the glycosylated form, SDG. Of plant lignans, MR produced the highest quantities of ENL: the quantity was over twofold compared with HMR or SDG. The majority of the animals, which had been given SECO, excreted higher quantities of END than ENL into urine, but ENL was the main lignan metabolite after SDG. The highest quantities of ENL in urine were measured after the administration of ENL as such. The (-)SECO isolated from Araucaria angustifolia was converted into (-)ENL only. The administration of (-)SDG, which was shown to produce (+)SECO, resulted in excretion of (+)ENL only and (-)HMR was converted into (-)ENL only. This confirmed that the absolute configurations at C8 and C8' are not changed during the microbial metabolism. Whether the biological effects are enantiomer-specific, remains to be resolved.

L5 ANSWER 18 OF 22 MEDLINE on STN DUPLICATE 7

2003059990. PubMed ID: 12570335. Antioxidant and antitumor effects of **hydroxymatairesinol** (HM-3000, HMR), a lignan isolated from the knots of spruce. Kangas Lauri; Saarinen Niina; Mutanen Marja; Ahotupa Markku; Hirsinummi Riikka; Unkila Mikko; Perala Merja; Soininen Pasi; Laatikainen Reino; Korte Helena; Santti Risto. (Hormos Nutraceutical Ltd, Turku, Finland.) European journal of cancer prevention : official journal of the European Cancer Prevention Organisation (ECP), (2002 Aug) 11 Suppl 2 S48-57. Journal code: 9300837. ISSN: 0959-8278. Pub. country: England: United Kingdom. Language: English.

AB The antioxidant properties of **hydroxymatairesinol** (HM-3000) were studied in vitro in lipid peroxidation, superoxide and peroxyl radical scavenging, and LDL-oxidation models in comparison with the known synthetic antioxidants Trolox (a water-soluble vitamin E derivative), butylated hydroxyanisol (BHA) and butylated hydroxytoluene (BHT). On a molar basis HM-3000 was a more effective antioxidant than Trolox in all assays and more effective than BHT or BHA in lipid peroxidation and superoxide scavenging test. The in vivo antioxidative effect (evaluated as the weight gain of C57BL/6J mice fed an alpha-tocopherol-deficient diet) of HM-3000 (500 mg/kg per day) was comparable to that of DL-alpha-tocopherol (766 mg/kg per day). The antitumor activity of HM-3000 was studied in dimethylbenz[a]anthracene (DMBA)-induced rat mammary cancer. HM-3000 had a statistically significant inhibitory effect on tumor growth. Prevention of tumor formation was also evaluated in the Apc(Min) mice model, which develops intestinal polyps spontaneously. HM-3000 was given in diet at 30 mg/kg per day and decreased the formation of polyps and prevented beta-catenin accumulation into the nucleus, the pathophysiological hallmark of polyp formation in this mouse model. In short-term toxicity studies (up to 28 days) HM-3000 was essentially non-toxic when given p.o. to rats and dogs (daily doses up to 2000 and 665 mg/kg, respectively); HM-3000 was shown to be well absorbed (> 50% of the dose) and rapidly eliminated. In human studies HM-3000 has been given in single doses up to 1350 mg to healthy male volunteers without treatment-related adverse events. Rapid absorption from the gastrointestinal tract and partial metabolism to **enterolactone** in humans was demonstrated. In summary, HM-3000 is a safe, novel **enterolactone** precursor lignan with antioxidant and antitumor properties.

L5 ANSWER 19 OF 22 MEDLINE on STN DUPLICATE 8

2001423900. PubMed ID: 11453749. In vitro metabolism of plant lignans: new precursors of mammalian lignans **enterolactone** and enterodiol. Heinonen S; Nurmi T; Liukkonen K; Poutanen K; Wahala K; Deyama T; Nishibe S; Adlercreutz H. (Folkhalsan Research Center and Department of Clinical Chemistry, P.O. Box 60, FIN-00014 University of Helsinki, Finland.) Journal of agricultural and food chemistry, (2001 Jul) 49 (7) 3178-86. Journal code: 0374755. ISSN: 0021-8561. Pub. country: United States. Language: English.

AB The metabolism of the plant lignans matairesinol, secoisolariciresinol,

pinoresinol, syringaresinol, arctigenin, 7-**hydroxymatairesinol**, isolariciresinol, and lariciresinol by human fecal microflora was investigated to study their properties as mammalian lignan precursors. The quantitative analyses of lignan precursors and the mammalian lignans **enterolactone** and enterodiol were performed by HPLC with coulometric electrode array detector. The metabolic products, including mammalian lignans, were characterized as trimethylsilyl derivatives by gas chromatography-mass spectrometry. Matairesinol, secoisolariciresinol, lariciresinol, and pinoresinol were converted to mammalian lignans only. Several metabolites were isolated and tentatively identified as for syringaresinol and arctigenin in addition to the mammalian lignans. Metabolites of 7-**hydroxymatairesinol** were characterized as **enterolactone** and 7-hydroxyenterolactone by comparison with authentic reference compounds. A metabolic scheme describing the conversion of the most abundant new mammalian lignan precursors, pinoresinol and lariciresinol, is presented.

L5 ANSWER 20 OF 22 MEDLINE on STN DUPLICATE 9

2002351838. PubMed ID: 12094633. Uptake and metabolism of **hydroxymatairesinol** in relation to its anticarcinogenicity in DMBA-induced rat mammary carcinoma model. Saarinen N M; Huovinen R; Warri A; Makela S I; Valentin-Blasini L; Needham L; Eckerman C; Collan Y U; Santti R. (Department of Anatomy, Institute of Biomedicine, University of Turku, FIN-20520 Turku, Finland.) Nutrition and cancer, (2001) 41 (1-2) 82-90. Journal code: 7905040. ISSN: 0163-5581. Pub. country: United States. Language: English.

AB The chemopreventive effects of **hydroxymatairesinol** (HMR), a lignan extracted from Norway spruce (Picea abies), on the development of mammary carcinoma induced by 7,12-dimethylbenz[a]anthracene (DMBA) was studied in rats. HMR administered via diet in an average daily dose of 4.7 mg/kg body wt starting before DMBA induction reduced tumor volume and tumor growth, but no significant reduction in tumor multiplicity (number of tumors/rat) was observed. The predominant histological type in the control group was type B (well-differentiated adenocarcinoma, 78%). The proportion of type B tumors decreased to 35% in the HMR group, while the type A (poorly differentiated) and type C (atrophic) tumor proportions increased. Anticarcinogenic effects of dietary HMR (4.7 mg/kg) were also evident when the administration started after DMBA induction and was seen as growth inhibition of established tumors. Dietary HMR supplementation significantly increased serum and urinary **enterolactone** and HMR concentrations but had no significant effect on the uterine weight, suggesting that HMR or its major metabolite **enterolactone** did not have an antiestrogenic effect. Further studies are warranted to further clarify and verify HMR action and the associated mechanisms in mammary tumorigenesis.

L5 ANSWER 21 OF 22 CAPLUS COPYRIGHT 2004 ACS on STN

2000:725669 Document No. 133:286508 **Hydroxymatairesinol** preparations in cancer prevention. Ahotupa, Markku; Eckerman, Christer; Kangas, Lauri; Makela, Sari; Saarinen, Niina; Santti, Risto; Warri, Anni (Hormos Nutraceutical Oy Ltd., Finland). PCT Int. Appl. WO 2000059946 A1 20001012, 43 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-FI181 20000309. PRIORITY: US 1999-281094 19990330.

AB This invention relates to methods for prevention of cancers, certain non-cancer, hormone dependent diseases and/or cardiovascular diseases in a person, based on administering of **hydroxymatairesinol** to said person. The invention also concerns a method for increasing the level of **enterolactone** or another metabolite of **hydroxymatairesinol**

in a person's serum thereby causing prevention of a cancer or a certain non-cancer, hormone dependent disease in a person, based on administering of **hydroxymatairesinol** to said person. Furthermore, this invention relates to pharmaceutical prepns., food additives and food products comprising **hydroxymatairesinol.**

L5 ANSWER 22 OF 22 MEDLINE on STN DUPLICATE 10
2001103469. PubMed ID: 10890032. **Hydroxymatairesinol**, a novel **enterolactone** precursor with antitumor properties from coniferous tree (Picea abies). Saarinen N M; Warri A; Makela S I; Eckerman C; Reunanen M; Ahotupa M; Salmi S M; Franke A A; Kangas L; Santti R. (Department of Anatomy, University of Turku, Finland.) Nutrition and cancer, (2000) 36 (2) 207-16. Journal code: 7905040. ISSN: 0163-5581. Pub. country: United States. Language: English.
AB The potential for the extraction of the plant lignan **hydroxymatairesinol** (HMR) in large scale from Norway spruce (Picea abies) has given us the opportunity to study the metabolism and biological actions of HMR in animals. HMR, the most abundant single component of spruce lignans, was metabolized to **enterolactone** (ENL) as the major metabolite in rats after oral administration. The amounts of urinary ENL increased with the dose of HMR (from 3 to 50 mg/kg), and only minor amounts of unmetabolized HMR isomers and other lignans were found in urine. HMR (15 mg/kg body wt po) given for 51 days decreased the number of growing tumors and increased the proportion of regressing and stabilized tumors in the rat dimethylbenz[a]anthracene-induced mammary tumor model. HMR (50 mg/kg body wt) did not exert estrogenic or antiestrogenic activity in the uterine growth test in immature rats. HMR also showed no antiandrogenic responses in the growth of accessory sex glands in adult male rats. Neither ENL nor enterodiol showed estrogenic or antiestrogenic activity via a classical alpha- or beta-type estrogen receptor-mediated pathway in vitro at < 1.0 microM. HMR was an effective antioxidant in vitro.

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L6 69 L1 AND MATAIRESINOL

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L7 ANSWER 1 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
2004:203863 Document No. 140:219654 Lignan complexes with cyclodextrins and their uses in food products, dietary supplements or pharmaceutical compositions. Jaervinen, Tomi; Jarho, Pekka; Unkila, Mikko; Hiilovaara-teijo, Mervi (Hormos Medical Corporation, Finland). PCT Int. Appl. WO 2004020474 A1 20040311, 26 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-FI511 20030624. PRIORITY: FI 2002-1545 20020829.
AB This invention concerns an inclusion complex of a lignan or lignan ester with a cyclodextrin. Furthermore, the invention concerns food products, dietary supplements or pharmaceutical compns. comprising said complex.

L7 ANSWER 2 OF 48 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN
2004:422662 The Genuine Article (R) Number: 815JG. Radical carboxyarylation

approach to lignans. Total synthesis of (-)-arctigenin, (-)-**matairesinol**, and related natural products. Fischer J (Reprint); Reynolds A J; Sharp L A; Sherburn M S. Univ Sydney, Sch Chem, Sydney, NSW 2006, Australia (Reprint); Australian Natl Univ, Res Sch Chem, Canberra, ACT 0200, Australia. ORGANIC LETTERS (29 APR 2004) Vol. 6, No. 9, pp. 1345-1348. Publisher: AMER CHEMICAL SOC. 1155 16TH ST, NW, WASHINGTON, DC 20036 USA. ISSN: 1523-7060. Pub. country: Australia. Language: English. *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*

AB Total syntheses of seven biologically important lignan natural products, including (-)-arctigenin, (-)-**matairesinol**, and (-)-alpha-conidendrin, by way of a highly stereoselective domino radical sequence is presented. The reported stereochemistry of the natural product 7-hydroxyarctigenin is shown to be erroneous; a diastereoisomeric structure is assigned to the natural product.

L7 ANSWER 3 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN

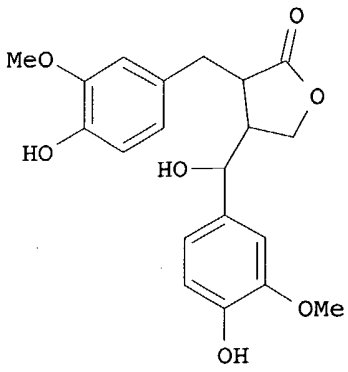
2004:437877 Document No. 141:99221 Chemopreventive effects of **hydroxymatairesinol** on uterine carcinogenesis in Donryu rats. Katsuda, Shin-ichi; Yoshida, Midori; Saarinen, Niina; Smeds, Annika; Nakae, Dai; Santti, Risto; Maekawa, Akihiko (Department of Biological Safety Research, Japan Food Research Laboratories, Tama, 206-0025, Japan). Experimental Biology and Medicine (Maywood, NJ, United States), 229(5), 417-424 (English) 2004. CODEN: EBMMBE. ISSN: 1535-3702. Publisher: Society for Experimental Biology and Medicine.

AB **Hydroxymatairesinol** (HMR), obtained from the heartwood of spruce (Picea abies), has been demonstrated to exert chemopreventive effects on the development of mammary tumors in rats. To examine the influence of HMR on uterine carcinogenesis, adult Donryu rats were initiated with a single intrauterine treatment of N-ethyl-N'-nitro-N-nitrosoguanidine (ENNG) at 11 wk of age and fed thereafter 0, 200, or 600 ppm HMR mixed in the soy-containing diet until 15 mo of age. Incidences of uterine adenocarcinoma in both 200 and 600 ppm HMR-dosed groups were significantly reduced to 11% and 15%, resp., <50% of 0 ppm, at the end of the experiment ($P < 0.05$). A delay in the start of persistent estrus by HMR was observed at 8 mo of age compared with controls given carcinogen alone. From urinalysis, HMR was metabolized mainly to enterolactone and hydroxyenterolactone. These findings suggest that HMR or its metabolites exert chemopreventive effects in the rat ENNG-uterine carcinogenesis model.

L7 ANSWER 4 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN

2004:2687 Document No. 140:65203 Lignan topical formulations. Korte, Helena; Lehtola, Veli-Matti; Unkila, Mikko; Hiilovaara-Teijo, Mervi; Ahotupa, Markku (Hormos Nutraceutical Oy Ltd., Finland). PCT Int. Appl. WO 2004000304 A1 20031231, 25 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-FI375 20030515. PRIORITY: FI 2002-1184 20020619.

GI



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AB This invention concerns a topical formulation comprising a lignan or lignan ester in a dermatol. acceptable vehicle. The formulation can be either a cosmetic formulation or a pharmaceutical formulation. E.g., water-in-oil emulsions contained a lignan such as **hydroxymatairesinol** (I) or **matairesinol** dibutyrate, an emulsifier such as sorbitan fatty acid ester, humectant such as glycerol, preservative, and water.

L7 ANSWER 5 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN

2003:633624 Document No. 139:179926 Preparation of lignan ester derivatives for use in pharmaceutical compositions and dietary supplements. Eklund, Patrik; Hiilovaara-Teijo, Mervi; Kalapudas, Arja; Kangas, Lauri; Lindholm, Anna; Sjoeholm, Rainer; Soedervall, Marja; Unkila, Mikko (Hormos Nutraceutical Oy Ltd., Finland). PCT Int. Appl. WO 2003066556 A1 20030814, 35 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-FI41 20030121. PRIORITY: FI 2002-222 20020205; FI 2002-563 20020325.

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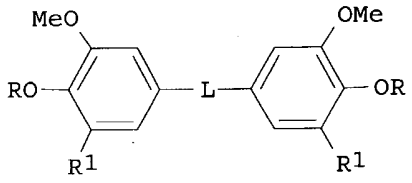

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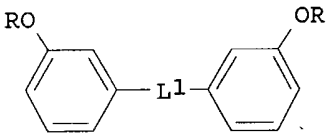
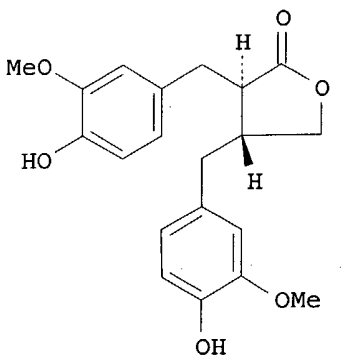


II

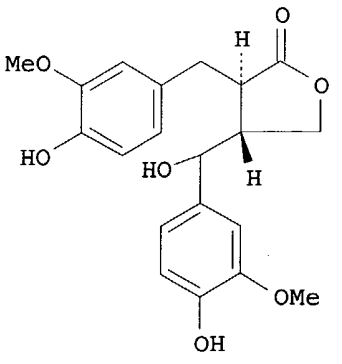
AB The invention relates to novel phenolic esters of lignans I (R = COR', SO2R'; R1 = H, OMe; R' = (un)substituted C1-22-alkyl, alkenyl, arylalkyl, aralkenyl, aromatic (substituted with OH, carboxyl, oxo, amino); L = skeleton of **hydroxymatairesinol**, **matairesinol**, lariciresinol, secoisolariciresinol, isolariciresinol, oxomatairesinol, α-conidendrin, pinoresinol, liovil, picearesinol, arctigenin, syringaresinol, nortrachelogenin) and II (L1 = enterodiol, R ≠ Ac, COEt; L1 = enterolactone), their geometric or stereoisomers. Thus, **matairesinol** dibutyrate was prepared from **matairesinol** via acylation with EtCOCl in CH2Cl2 containing pyridine. Furthermore, the invention concerns pharmaceutical compns., dietary supplements, and food products comprising said esters.

L7 ANSWER 6 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
2003:551373 Document No. 139:117267 Preparation of **matairesinol** from **hydroxymatairesinol.** Sjoeholm, Rainer; Eklund, Patrik; Mikkola, Jyri-pekka; Lehtilae, Reko; Soedervall, Marja; Kalapudas, Arja (Hormos Nutraceutical Oy Ltd., Finland). PCT Int. Appl. WO 2003057209 A1 20030717, 26 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-FI1 20030102. PRIORITY: FI 2002-32 20020109; FI 2002-235 20020206.

GI



I



II

AB The present invention concerns a method for the preparation of **matairesinol** (I) from **hydroxymatairesinol** (II), either by (i) catalytic hydrogenolysis of the hydroxy group in 7-position of II, wherein the reaction is carried out in a suitable solvent as a pressurized hydrogenolysis, or (ii) reduction of II, wherein the reduction is carried out as a hydrogen transfer reaction from a hydrogen donor in the presence of a catalyst.

L7 ANSWER 7 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
2003:590821 Document No. 139:128028 Method for prevention of diseases in coeliac patients. Unkila, Mikko (Finland). U.S. Pat. Appl. Publ. US 2003144216 A1 20030731, 5 pp. (English). CODEN: USXXCO. APPLICATION: US 2002-54900 20020125.

AB Methods for prevention of cancers, precancers, certain non-cancer, hormone dependent diseases and/or cardiovascular diseases in a person suffering from coeliac disease, based on administering of a lignan to the person. A method for increasing the level of enterolactone or another metabolite of a lignan in a person's serum is also disclosed, where the person suffers from coeliac disease, thereby causing prevention of a cancer or a certain non-cancer, hormone dependent disease in the person, based on administering of a lignan to the person.

L7 ANSWER 8 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
2003:414080 Document No. 138:379228 Method using lignans for inhibiting overactivity of phagocytes or lymphocytes in an individual, and therapeutic use. Ahotupa, Markku; Eriksson, John; Kangas, Lauri; Unkila, Mikko; Komi, Janne; Perala, Merja; Korte, Helena (Finland). U.S. Pat. Appl. Publ. US 2003100514 A1 20030529, 10 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-991971 20011126.

AB The invention provides a method for inhibiting the overactivity of phagocytes or lymphocytes in an individual by administering to the individual an effective amount of a lignan, wherein (i) the phagocytes are neutrophils and the lignan is **hydroxymatairesinol** or **matairesinol** or mixts. thereof; or (ii) the phagocytes are cells of myeloid origin and the lignan is enterolactone or **hydroxymatairesinol** or mixts. thereof; or (iii) the lymphocytes are T-lymphocytes and the lignan is **hydroxymatairesinol**, **matairesinol** or enterolactone or mixts. thereof. The invention also provides a method for treating or preventing an acute ischemia-reperfusion injury or a chronic condition, caused by overactivity of phagocytes or lymphocytes in an individual, the method comprising decreasing the activity of phagocytes in an individual by administering to the individual an effective amount of a lignan.

L7 ANSWER 9 OF 48 MEDLINE on STN DUPLICATE 1
2003073811. PubMed ID: 12583751. Synthesis of (-)-**matairesinol**, (-)-enterolactone, and (-)-enterodiol from the natural lignan

hydroxymatairesinol. Eklund Patrik; Lindholm Anna; Mikkola J-P; Smeds Annika; Lehtila Reko; Sjoholm Rainer. (Department of Organic Chemistry, Abo Akademi University, Biskopsgatan 8, 20500-FIN, Abo, Finland.. paeklund@abo.fi) . Organic letters, (2003 Feb 20) 5 (4) 491-3. Journal code: 100890393. ISSN: 1523-7060. Pub. country: United States. Language: English.

AB [reaction: see text] We describe here a four-step semisynthetic method for the preparation of enantiomerically pure (-)-enterolactone starting from the readily available lignan **hydroxymatairesinol** from Norway spruce (Picea abies). **Hydroxymatairesinol** was first hydrogenated to **matairesinol. Matairesinol** was esterified to afford the matairesinyl 4,4'-bistriflate, which was deoxygenated by palladium-catalyzed reduction to 3,3'-dimethylenterolactone. Demethylation of 3,3'-dimethylenterolactone and reduction with LiAlH(4) yielded (-)-enterolactone and (-)-enterodiol, respectively.

L7 ANSWER 10 OF 48 MEDLINE on STN DUPLICATE 2

2003372627. PubMed ID: 12906904. Liquid chromatographic-tandem mass spectrometric method for the plant lignan 7-**hydroxymatairesinol** and its potential metabolites in human plasma. Smeds Annika; Hakala Kristo. (Abo Akademi University, Department of Organic Chemistry, Biskopsgatan 8, FIN-20500, Turku, Finland.. ansmeds@abo.fi) . Journal of chromatography. B, Analytical technologies in the biomedical and life sciences, (2003 Aug 15) 793 (2) 297-308. Journal code: 101139554. ISSN: 1570-0232. Pub. country: United States. Language: English.

AB A HPLC-MS-MS method was developed for the determination of the plant lignan 7-**hydroxymatairesinol** and its potential metabolites **matairesinol**, oxomatairesinol, alpha-conidendrin, 7-hydroxyenterolactone, enterodiol, and enterolactone in human plasma. The method included sample cleanup by solid-phase extraction (SPE) and analysis using a PE Sciex API3000 triple quadrupole mass spectrometer with electrospray ionisation. The lignans were quantified using two deuterated internal standards. They showed good chromatographic linearity, analysis repeatability, and SPE recovery in the presence of plasma. In pooled plasma and in plasma samples collected from two individual subjects lignan glucuronides and sulfates were enzymatically hydrolysed to free lignans and then analysed. All the lignans could be detected in the samples.

L7 ANSWER 11 OF 48 EMBASE on STN

2003267147 EMBASE Bioavailability of phyto-oestrogens. Rowland I.; Faughnan M.; Hoey L.; Wahala K.; Williamson G.; Cassidy A.. Dr. I. Rowland, Northern Ireland Ctr. for Food/Hlth., University of Ulster, Coleraine BT52 1SA, United Kingdom. i.rowland@ulst.ac.uk. British Journal of Nutrition 89/SUPPL. 1 (S45-S58) 1 Jun 2003.
Refs: 81.
ISSN: 0007-1145. CODEN: BJNUAV. Pub. Country: United Kingdom. Language: English. Summary Language: English.

AB The term phyto-oestrogen encompasses isoflavone compounds, such as genistein and daidzein, found predominantly in soya products and the lignans, such as **matairesinol** and secoisolariciresinol, found in many fruits, cereals and in flaxseed. There is evidence that they have potential health benefits in man particularly against hormone-dependent diseases such as breast and prostate cancers and osteoporosis. This has led to intense interest in their absorption and biotransformation in man. The metabolism of isoflavones and lignans in animals and man is complex and involves both mammalian and gut microbial processes. Isoflavones are present predominantly as glucosides in most commercially available soya products; there is evidence that they are not absorbed in this form and that their bioavailability requires initial hydrolysis of the sugar moiety by intestinal β-glucosidases. After absorption, phyto-oestrogens are reconjugated predominantly to glucuronic acid and to a lesser degree to sulphuric acid. Only a small portion of the free aglycone has been detected in blood, demonstrating that the rate of conjugation is high.

There is extensive further metabolism of isoflavones (to equol and O-desmethyl-angolensin) and lignans (to enterodiol and enterolactone) by gut bacteria. In human subjects, even those on controlled diets, there is large interindividual Variation in the metabolism of isoflavones and lignans, particularly in the production of the gut bacterial metabolite equol (from daidzein). Factors influencing absorption and metabolism of phyto-oestrogens include diet and gut microflora.

L7 ANSWER 12 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
2003:156594 Document No. 139:8300 Lignans and lipophilic extractives in Norway spruce knots and stemwood. Willfor, Stefan; Hemming, Jarl; Reunanen, Markku; Eckerman, Christer; Holmbom, Bjarne (Process Chemistry Group, Abo Akademi University, Turku/Abo, Finland). Holzforschung, 57(1), 27-36 (English) 2003. CODEN: HOLZAZ. ISSN: 0018-3830. Publisher: Walter de Gruyter GmbH & Co. KG.
AB The hydrophilic and lipophilic extractives in the heartwood of knots from 7 Norway spruce trees were analyzed by GC, GC-MS and HPSEC. The knots contained extremely large amts. of lignans, 6-24% (weight/weight), with **hydroxymatairesinol** comprising 65-85% of the lignans. Even the knots of the young trees contained 4-8% (weight/weight) of lignans. The variation in the amount of lignans was large among knots, both within a single tree and between trees. In addition to the lignans, knots also contained 2-6% (weight/weight) of a complex mixture of lignan-like compds. with 3, 4 and even up to 6 Ph propane units, here called oligolignans. The amts. of lignans in the knots were similar in the radial direction from the pith into the outer branch, but decreased dramatically outwards in the branch, almost disappearing after 10-20 cm. The ratio of the 2 epimers of **hydroxymatairesinol** differed between different knots and even within the knot. A new spruce lignan, nortrachelogenin, or its enantiomer, wikstromol, was detected in knots from trees in northern Finland as opposed to samples from southern Finland. The amount of lipophilic extractives was small compared to the amount of hydrophilic extractives in the knots. Five of the dead knots contained more resin acids and free diterpenyl alcs. than ordinary stemwood. In the other knots, the amount of lipophilic extractives was on the same level as stem heartwood. The stem sapwood contained larger amts. of esterified fatty acids than the knots.

L7 ANSWER 13 OF 48 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
2003267142 EMBASE Analysis of phyto-oestrogens in biological matrices. Hoikkala A.A.; Schiavoni E.; Wahala K.. Prof. K. Wahala, Department of Chemistry, Laboratory of Organic Chemistry, University of Helsinki, PO Box 55, FIN-00014 Helsinki, Finland. kristiina.wahala@helsinki.fi. British Journal of Nutrition 89/SUPPL. 1 (S5-S18) 1 Jun 2003.
Refs: 95.
ISSN: 0007-1145. CODEN: BJNUAV. Pub. Country: United Kingdom. Language: English. Summary Language: English.
AB A review covering different methods for the analysis of phyto-oestrogens in biological matrices is presented. Sample pretreatment and analysis of isoflavonoids and lignans by HPLC and GC with various detection methods are discussed. The immunoassay method is also briefly presented.

L7 ANSWER 14 OF 48 MEDLINE on STN DUPLICATE 3
2002484700. PubMed ID: 12270222. Structural determinants of plant lignans for the formation of enterolactone in vivo. Saarinen Niina M; Smeds Annika; Makela Sari I; Ammala Jenni; Hakala Kristo; Pihlava Juha-Matti; Ryhanen Eeva-Liisa; Sjoholm Rainer; Santti Risto. (Department of Anatomy, Institute of Biomedicine, University of Turku, FIN-20520, Turku, Finland.) Journal of chromatography. B, Analytical technologies in the biomedical and life sciences, (2002 Sep 25) 777 (1-2) 311-9. Journal code: 101139554. ISSN: 1570-0232. Pub. country: United States. Language: English.
AB The quantity of mammalian lignans enterolactone (ENL) and enterodiol (END)

and of plant lignans secoisolariciresinol (SECO) and 7-**hydroxymatairesinol** (HMR) excreted in a 24-h rat urine sample was measured after a single p.o. dose of an equivalent quantity of secoisolariciresinol diglycoside (SDG), secoisolariciresinol (SECO), **matairesinol** (MR), 7-**hydroxymatairesinol** (HMR) and ENL. Plant lignans (SECO and HMR) were partially absorbed as such. The aglycone form of SECO was more efficiently converted into mammalian lignans END and ENL than the glycosylated form, SDG. Of plant lignans, MR produced the highest quantities of ENL: the quantity was over twofold compared with HMR or SDG. The majority of the animals, which had been given SECO, excreted higher quantities of END than ENL into urine, but ENL was the main lignan metabolite after SDG. The highest quantities of ENL in urine were measured after the administration of ENL as such. The (-)SECO isolated from Araucaria angustifolia was converted into (-)ENL only. The administration of (-)SDG, which was shown to produce (+)SECO, resulted in excretion of (+)ENL only and (-)HMR was converted into (-)ENL only. This confirmed that the absolute configurations at C8 and C8' are not changed during the microbial metabolism. Whether the biological effects are enantiomer-specific, remains to be resolved.

L7 ANSWER 15 OF 48 MEDLINE on STN DUPLICATE 4

2001423900. PubMed ID: 11453749. In vitro metabolism of plant lignans: new precursors of mammalian lignans enterolactone and enterodiol. Heinonen S; Nurmi T; Liukkonen K; Poutanen K; Wahala K; Deyama T; Nishibe S; Adlercreutz H. (Folkhalsan Research Center and Department of Clinical Chemistry, P.O. Box 60, FIN-00014 University of Helsinki, Finland.) Journal of agricultural and food chemistry, (2001 Jul) 49 (7) 3178-86. Journal code: 0374755. ISSN: 0021-8561. Pub. country: United States. Language: English.

AB The metabolism of the plant lignans **matairesinol**, secoisolariciresinol, pinoresinol, syringaresinol, arctigenin, 7-**hydroxymatairesinol**, isolariciresinol, and lariciresinol by human fecal microflora was investigated to study their properties as mammalian lignan precursors. The quantitative analyses of lignan precursors and the mammalian lignans enterolactone and enterodiol were performed by HPLC with coulometric electrode array detector. The metabolic products, including mammalian lignans, were characterized as trimethylsilyl derivatives by gas chromatography-mass spectrometry. **Matairesinol**, secoisolariciresinol, lariciresinol, and pinoresinol were converted to mammalian lignans only. Several metabolites were isolated and tentatively identified as for syringaresinol and arctigenin in addition to the mammalian lignans. Metabolites of 7-**hydroxymatairesinol** were characterized as enterolactone and 7-hydroxyenterolactone by comparison with authentic reference compounds. A metabolic scheme describing the conversion of the most abundant new mammalian lignan precursors, pinoresinol and lariciresinol, is presented.

L7 ANSWER 16 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN

2002:543197 Document No. 137:216291 Uptake and metabolism of **hydroxymatairesinol** in relation to its anticarcinogenicity in DMBA-induced rat mammary carcinoma model. Saarinen, Niina M.; Huovinen, Riikka; Waerri, Anni; Maekelae, Sari I.; Valentin-Blasini, Liza; Needham, Larry; Eckerman, Christer; Collan, Yrjoe U.; Santti, Risto (Department of Anatomy, Institute of Biomedicine, University of Turku, Turku, FIN-20520, Finland). Nutrition and Cancer, 41(1&2), 82-90 (English) 2001. CODEN: NUCADQ. ISSN: 0163-5581. Publisher: Lawrence Erlbaum Associates, Inc..

AB The chemopreventive effects of **hydroxymatairesinol** (HMR), a lignan extracted from Norway spruce (Picea abies), on the development of mammary carcinoma induced by 7,12-dimethylbenz[a]anthracene (DMBA) was studied in rats. HMR administered via diet in an average daily dose of 4.7 mg/kg body wt starting before DMBA induction reduced tumor volume and tumor growth, but no significant reduction in tumor multiplicity (number of tumors/rat) was observed The predominant histol. type in the control group was type B (well-differentiated adenocarcinoma, 78%). The proportion of type B

tumors decreased to 35% in the HMR group, while the type A (poorly differentiated) and type C (atrophic) tumor proportions increased. Anticarcinogenic effects of dietary HMR (4.7 mg/kg) were also evident when the administration started after DMBA induction and was seen as growth inhibition of established tumors. Dietary HMR supplementation significantly increased serum and urinary enterolactone and HMR concns. but had no significant effect on the uterine weight, suggesting that HMR or its major metabolite enterolactone did not have an anti-estrogenic effect. Further studies are warranted to further clarify and verify HMR action and the associated mechanisms in mammary tumorigenesis.

L7 ANSWER 17 OF 48 MEDLINE on STN DUPLICATE 5

2001129080. PubMed ID: 11130663. Dirigent-mediated podophyllotoxin biosynthesis in Linum flavum and Podophyllum peltatum. Xia Z Q; Costa M A; Proctor J; Davin L B; Lewis N G. (Institute of Biological Chemistry, Washington State University, Pullman 99164-6340, USA.) Phytochemistry, (2000 Nov) 55 (6) 537-49. Journal code: 0151434. ISSN: 0031-9422. Pub. country: United States. Language: English.

AB Given the importance of the antitumor/antiviral lignans, podophyllotoxin and 5-methoxypodophyllotoxin, as biotechnological targets, their biosynthetic pathways were investigated in Podophyllum peltatum and Linum flavum. Entry into their pathways was established to occur via dirigent mediated coupling of E-coniferyl alcohol to afford (+)-pinoresinol; the encoding gene was cloned and the recombinant protein subsequently obtained. Radiolabeled substrate studies using partially purified enzyme preparations next revealed (+)-pinoresinol was enantiospecifically converted sequentially into (+)-lariciresinol and (-)-secoisolariciresinol via the action of an NADPH-dependent bifunctional pinoresinol/lariciresinol reductase. The resulting (-)-secoisolariciresinol was enantiospecifically dehydrogenated into (-)-**matairesinol**, as evidenced through the conversion of both radio- and stable isotopically labeled secoisolariciresinol into **matairesinol**, this being catalyzed by the NAD-dependent secoisolariciresinol dehydrogenase. (-)-**Matairesinol** was further hydroxylated to afford 7'-**hydroxymatairesinol**, this being efficiently metabolized into 5-methoxypodophyllotoxin. Thus much of the overall biosynthetic pathway to podophyllotoxin has been established, that is, from the dirigent mediated coupling of E-coniferyl alcohol to the subsequent conversions leading to 7'-**hydroxymatairesinol.**

L7 ANSWER 18 OF 48 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN DUPLICATE 6

2000415530 EMBASE Chemopreventive activity of crude hydroxsymatairesinol (HMR) extract in Apc(Min) mice. Oikarinen S.I.; Pajari A.-M.; Mutanen M.. M. Mutanen, Dept. of Applied Chem./Microbiol., University of Helsinki, P.O. Box 27, FIN-00014, Helsinki, Finland. marja.mutanen@helsinki.fi. Cancer Letters 161/2 (253-258) 20 Dec 2000.
Refs: 18.
ISSN: 0304-3835. CODEN: CALEDQ.
Publisher Ident.: S 0304-3835(00)00543-7. Pub. Country: Ireland. Language: English. Summary Language: English.

AB We studied the effects of a lignan, **hydroxymatairesinol** (HMR), and rye bran on intestinal tumor development in adenomatous polyposis colimultiple intestinal neoplasia (Apc)(Min) mice. HMR showed a strong chemopreventive effect in this animal model. The mean number of adenomas in the small intestine was significantly lower (26.6 ± 11.0, $P < 0.05$) in mice fed the inulin and HMR when compared with the inulin and inulin/rye bran fed mice (39.6 ± 8.9 and 36.0 ± 7.4, respectively). HMR resulted in normalization of β-catenin levels in adenoma tissue, indicating that HMR mediates its chemopreventive effect through the Apc-β-catenin pathway. In the cytosolic fraction, β-catenin level in adenoma tissue was significantly elevated ($P = 0.008$-0.013) in all the diet groups as compared with that of the surrounding mucosa. In the nuclear fraction, β-catenin in the inulin (3.15 ± 2.9 relative units) and inulin/rye (5.17 ± 6.94 relative units) groups was also

significantly higher (P = 0.003-0.009) in the adenoma tissue when compared with the surrounding mucosa (0.5 ± 0.5 and 0.35 ± 0.39 relative units). However, HMR was able to restore nuclear β-catenin level of the adenoma tissue (0.41 ± 0.25 relative units) to the level found in the surrounding mucosa (0.36 ± 0.28 relative units). (C) 2000 Published Elsevier Science Ireland Ltd.

L7 ANSWER 19 OF 48 MEDLINE on STN DUPLICATE 7

2001103469. PubMed ID: 10890032. **Hydroxymatairesinol**, a novel enterolactone precursor with antitumor properties from coniferous tree (Picea abies). Saarinen N M; Warri A; Makela S I; Eckerman C; Reunanen M; Ahotupa M; Salmi S M; Franke A A; Kangas L; Santti R. (Department of Anatomy, University of Turku, Finland.) Nutrition and cancer, (2000) 36 (2) 207-16. Journal code: 7905040. ISSN: 0163-5581. Pub. country: United States. Language: English.

AB The potential for the extraction of the plant lignan **hydroxymatairesinol** (HMR) in large scale from Norway spruce (Picea abies) has given us the opportunity to study the metabolism and biological actions of HMR in animals. HMR, the most abundant single component of spruce lignans, was metabolized to enterolactone (ENL) as the major metabolite in rats after oral administration. The amounts of urinary ENL increased with the dose of HMR (from 3 to 50 mg/kg), and only minor amounts of unmetabolized HMR isomers and other lignans were found in urine. HMR (15 mg/kg body wt po) given for 51 days decreased the number of growing tumors and increased the proportion of regressing and stabilized tumors in the rat dimethylbenz[a]anthracene-induced mammary tumor model. HMR (50 mg/kg body wt) did not exert estrogenic or antiestrogenic activity in the uterine growth test in immature rats. HMR also showed no antiandrogenic responses in the growth of accessory sex glands in adult male rats. Neither ENL nor enterodiol showed estrogenic or antiestrogenic activity via a classical alpha- or beta-type estrogen receptor-mediated pathway in vitro at < 1.0 microM. HMR was an effective antioxidant in vitro.

L7 ANSWER 20 OF 48 EMBASE on STN

2000340272 EMBASE Chemopreventive activity of hydroksymatairesinol in adenomatous polyposis colimultiple intestinal neoplasia (Apc)(Min) mice. Oikannen S.I.; Pajari A.-M.; Mutanen M.. M. Mutanen, Dept. of Appl. Chem. and Microbiol., University of Helsinki, P.O. Box 27, FIN-00014 Helsinki, Finland. maria.mutanenc@helsinki.fi. Cancer Letters 159/2 (183-187) 31 Oct 2000.

Refs: 15.

ISSN: 0304-3835. CODEN: CALEDQ.

Publisher Ident.: S 0304-3835(00)00543-7. Pub. Country: Ireland. Language: English. Summary Language: English.

AB We studied the effects of a lignan, **hydroxymatairesinol** (HMR), and rye bran on intestinal tumor development in adenomatous polyposis colimultiple intestinal neoplasia (Apc)(Min) mice. HMR showed a strong chemopreventive effect in this animal model. The mean number of adenomas in the small intestine was significantly lower (26.6 ± 11.0, P < 0.05) in mice fed the TNS tumor promoter insulin and HMR when compared with the insulin and insulin/rye bran fed mice (39.6 ± 8.9 and 36.0 ± 7.4, respectively). HMR resulted in normalization of β-catenin levels in adenoma tissue, indicating that HMR mediates its chemopreventive effect through the Apc-β-catenin pathway. In the cytosolic fraction, β-catenin level in adenoma tissue was significantly elevated (P = 0.008-0.013) in all the diet groups as compared with that of the surrounding mucosa. In the nuclear fraction, β-catenin in the insulin (3.15 ± 2.9 relative units) and insulin/rye (5.17 ± 6.94 relative units) groups was also significantly higher (P = 0.003-0.009) in the adenoma tissue when compared with the surrounding mucosa (0.5 ± 0.5 and 0.35 ± 0.39 relative units). However, HMR was able to restore nuclear β-catenin level of the adenoma tissue (0.41 ± 0.25 relative units) to the level found in the surrounding mucosa (0.36 ± 0.28 relative

units). (C) 2000 Published by Elsevier Science Ireland Ltd.

L7 ANSWER 21 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
1999:693513 Document No. 132:33212 Lignans, flavonoids and phenolic derivatives from Taxus mairei. Yang, Shung-Jim; Fang, Jim-Min; Cheng, Yu-Shia (Department of Chemistry, National Taiwan University, Taipei, 106, Taiwan). Journal of the Chinese Chemical Society (Taipei), 46(5), 811-818 (English) 1999. CODEN: JCCTAC. ISSN: 0009-4536. Publisher: Chinese Chemical Society.
AB From the twigs of Taxus mairei, 35 lignans, 2 sesquilignans, 4 flavonoids, 3 bisflavonoids, 13 phenolic derivs., 2 sesquiterpenes, 3 bisnorsesquiterpenes, 3 long-chain carboxylic acids and 4 steroids were isolated. The new lignans and phenolic glucosides include 7'-hydroxynortrachelogenin, 7-**hydroxymatairesinol**, 3'-O-demethylepipinoresinol, taxiresinol 9-acetate, 3'-O-demethyltanegool, 8'-epitanegool, 3,3'-dimethoxy-4,4',9-trihydroxy-7,9'-epoxylignan-7'-one, 3-O-demethyldihydrodehydrodiconiferyl alc., taxumaiglucoside A heptaacetate, taxumaiglucoside B heptaacetate, and taxumaiglucoside C heptaacetate. Their structures were determined by spectral methods.

L7 ANSWER 22 OF 48 SCISEARCH COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 8
94:740582 The Genuine Article (R) Number: PR974. THE EXTRACTIVES OF AOMORI TODOMATSU (ABIES-MARIESII MASTERS) - ISOLATIONS OF LIGNANS FROM THE HEARTWOOD. OMORI S (Reprint); OZAWA S; TANEDA K. SUNY SYRACUSE, COLL ENVIRONM SCI & FORESTRY, SYRACUSE, NY, 13210 (Reprint); IWATE UNIV, FAC AGR, MORIOKA, IWATE 020, JAPAN. MOKUZAI GAKKAISHI (1994) Vol. 40, No. 10, pp. 1107-1118. ISSN: 0021-4795. Pub. country: USA; JAPAN. Language: Japanese.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB This study examined the extractive components of Abies mariesii Masters (Aomori todomatsu). This hardy softwood species is grown primarily in the coldest region of the main island of Japan.

The ether and hexane soluble extractives from the heartwood of A. mariesii were determined. Ten compounds were identified from ether soluble fractions: alpha-conidendrin (I), **matairesinol** (II), ketomatairesinol (III), **hydroxymatairesinol** (IV), 1,2,3,4-tetrahydro-7-hydroxy-r-1-(4'-hydroxy-3'-methoxyphenyl)-t-2-hydroxymethyl-6-methoxy-c-3-naphthalenecarbaldehyde gamma-lactol (todolactol-B, V), t-4-(4'-hydroxy-3'-methoxybenzoyl)-r-2-(4''-hydroxy-3''-methoxyphenyl)-t-3-hydroxymethyl-tetrahydrofuran (VI), 2-hydroxy-t-4-[hydroxy(4'-hydroxy-3'-methoxyphenyl)methyl]-r-3-(4''-hydroxy-3''-methoxybenzyl)-tetrahydrofuran (todolactol-A, VII), t-4-(p-coumaroyloxy) (4'-hydroxy-3'-methoxyphenyl)methyl-2-hydroxy-r-3-(4''-hydroxy-3''-methoxybenzyl)-tetrahydrofuran (todolactol-A alpha'-p-coumarate, VIII),vanillic acid (IX),and t-4-[hydroxy (4'-hydroxy-3'-methoxyphenyl)methyl]-r-2-(4''-hydroxy-3''-methoxyphenyl)-t-3-hydroxymethyl-tetrahydrofuran (X), and beta-sitosterol (XI) was isolated and identified from the hexane soluble fraction. In this study the major features were a relatively large yield of **matairesinol** (II), comparable to that of compounds alpha-conidendrin (I) and **hydroxymatairesinol** (IV), and the presence of the lactol-type phenolic lignans such as Compounds (V), (VII), and (VIII).

L7 ANSWER 23 OF 48 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
94211290 EMBASE Document No.: 1994211290. Taxoids from the roots of Taxus x medica cv. Hicksii. Appendino G.; Cravotto G.; Enriu R.; Gariboldi P.; Barboni L.; Torregiani E.; et al.. Dipt. Scienza/Tecnologia del Farmaco, via Giuria 9,10125 Torino, Italy. Journal of Natural Products 57/5 (607-613) 1994.
ISSN: 0163-3864. CODEN: JNPRDF. Pub. Country: United States. Language: English. Summary Language: English.
AB The roots of Taxus x media cv. Hicksii gave two new pseudoalkaloidal taxoids, identified as N-debenzoyl-N-butanoyl taxol [1] and

7β-acetoxy-9- acetylspicataxine [2a]. A new baccatin IV derivative [7a] and the lignans **hydroxymatairesinol** [8] and (-)-epinortrachelogenin [9] were also isolated. The epoxidation of Δ(4(20),11) taxadienes was investigated, disclosing an unusual reactivity of the bridgehead double-bond towards peracids. Regiochemically and stereochemically unnatural epoxides of taxoids were obtained. Nmr data for these compounds were compared with literature values on the natural epoxides. No significant correlation between the configuration of the 4(20)-oxirane ring and the chemical shift of H-5 was found.

L7 ANSWER 24 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN

1990:79734 Document No. 112:79734 The wood extractives in alkaline peroxide bleaching of groundwood from Norway spruce. Ekman, Rainer; Holmbom, Bjarne (Lab. For. Prod. Chem., Abo Akad., Abo, SF-20500, Finland). Nordic Pulp & Paper Research Journal, 4(3), 188-91 (English) 1989. CODEN: NPPJEG. ISSN: 0283-2631.

AB The changes in extractive composition of groundwood pulp from Norway spruce upon alkaline H2O2 bleaching in a paper mill were investigated by gas chromatog. Only slight hydrolysis of esterified fatty acids occurred in bleaching and no significant alteration of the composition of the fatty acids was observed No changes were found in the amount and composition of free and esterified sterols. However, considerable oxidation of abietadienoic resin acids occurred whereas the pimaric-type resin acids and dehydroabietic acid were practically unaffected by bleaching. Among the polar extractives, the spruce lignans exhibited a drastic decrease including alkali-induced transformation of **hydroxymatairesinol** to conidendric acid. The spruce bark derived stilbenes were almost completely oxidized in bleaching. Alkaline H2O2 bleaching produced a series of aliphatic C2-C4 hydroxy and dicarboxylic acids. Glycolic, oxalic, 2-deoxytetronic and malic acids were the major components of this group.

L7 ANSWER 25 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN

1989:121412 Document No. 110:121412 Pharmaceuticals containing leucoanthocyans for the treatment of alcoholism. Brekhman, I. I.; Bulanov, A. E.; Polozhentseva, M. I.; Mudzhiri, L. A.; Alkhazashvili, G. G.; Kalatozishvili, E. I.; Dardymov, I. V.; Bezdetko, G. N.; Khasina, E. I. (Institute of Biology of the Sea, Vladivostok, USSR; Scientific-Research Institute of Horticulture, Viticulture, and Wine Making). Ger. Offen. DE 3641495 A1 19880609, 21 pp. (German). CODEN: GWXXBX. APPLICATION: DE 1986-3641495 19861204.

AB A pharmaceutical for the treatment of pathol. alc. addiction contains leucoanthocyans 219-270, catechins 153-187, flavonols 81-99, lignin 68-83, reducing saccharides 216-264, pectin 18-22, free amino acids 27-33, organic acids 36-44, sterols 4.5-5.5, methylsterols 1.35-1.65, dimethylsterols 1.98-2.42, lignans 13.5-16.5, lignan glycosides 9-11, phenolcarboxylic acids 13.5-16.5, phenolaldehydes 4.5-5.5, and alkyl ferulates 4.5-5.5 mg/g. Alc. rats received drinking water containing 15% EtOH and 1 mL/50 mL of the above mixture for 13 wk and were then kept abstinent for 10 days; in the abstinent animals the deprivation occurred without alc. withdrawal symptoms. Animals receiving the above mixture and free to choose water or 15% EtOH-containing water, decreased their EtOH consumption by 100% after the deprivation period, whereas alc. consumption increased in the control.

L7 ANSWER 26 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN

1985:593134 Document No. 103:193134 A study of the constituents of the heartwood of Tsuga chinensis Pritz. var. formosana (Hay.). Fang, Jim Min; Wei, Kuo Min; Cheng, Yu Shia (Dep. Chem., Natl. Taiwan Univ., Taipei, Taiwan). Journal of the Chinese Chemical Society (Taipei, Taiwan), 32(1), 75-80 (English) 1985. CODEN: JCCTAC. ISSN: 0009-4536.

AB By means of spectroscopic anal., x-ray crystallog., and chemical correlation the heartwood of Taiwan hemlock was found to contain sterols, carboxylic acids, 13-epimanool, o-methoxyphenolics, coniferaldehyde, benzofuranoid neolignan, α-conidendrin, tsugacetal, isolariciresinol, secoisolariciresinol, **matairesinol**, **hydroxymatairesinol** and oxomatairesinol. Among them (+)-tsugacetal is a novel lignan acetal

having an α-conidendrin-related structure with the acetal methoxy group at the β-position.

L7 ANSWER 27 OF 48 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

1982:255084 Document No.: PREV198274027564; BA74:27564. LIGNANS FROM TAXUS-WALLICHIANA. MILLER R W [Reprint author]; MCLAUGHLIN J L; POWELL R G; PLATTNER R D; WEISLEDER D; SMITH C R. NORTH REG RES CENT, AGRIC RES SERV, US DEP AGRIC, PEORIA, ILL 61604, USA. Journal of Natural Products (Lloydia), (1982) Vol. 45, No. 1, pp. 78-82.
CODEN: JNPRDF. ISSN: 0163-3864. Language: ENGLISH.

AB Three lignans were isolated from the roots, stems and needles of T. wallichiana Zucc. Two of these were identified as epimers of conidendrin and **hydroxymatairesinol.** The structure of the 3rd, a previously unknown lignan named isoliovil, was established by 1H and 13C NMR and mass spectrometry.

L7 ANSWER 28 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN

1982:102372 Document No. 96:102372 Spectrophotometric determination of lignans in oakwood and brandy spirits. Kuridze, M. G.; Leont'eva, V. G.; Mudzhiri, L. A.; Semenov, A. A.; Lashkhi, A. D. (Nauchno-Issled. Inst. Sadovod., Vinograd. Vinodel., Tbilisi, USSR). Izvestiya Akademii Nauk Gruzinskoi SSR, Seriya Khimicheskaya, 7(3), 213-23 (Russian) 1981. CODEN: IGSKDH. ISSN: 0132-6074.

AB To determine lignin [9005-53-2] components, a sample (100 mL brandy or alc. extract of oak wood) is concentrated, purified by column chromatog. on Chromaton N-AW, and resolved by TLC on silica gel. The individual components (secoisolariciresinol [29388-59-8], liovil [484-39-9], lariciresinol [27003-73-2], olivil [2955-23-9], pinoresinol [487-36-5], eudesmin [526-06-7], **matairesinol** [580-72-3], **hydroxymatairesinol** [20268-71-7], and isolariciresinol [548-29-8]) are sep. eluted with EtOH and the optical d. of each solution is measured in a spectrophotometer (SF-26) at the appropriate wavelength in the UV region. The amount of lignin component is computed from a calibration curve. The relative error of the method was ≤1.88%. The total lignin content in brandy increased upon storage from 41.4 mg/L (after 1 yr) to 140.9 mg/mL (after 20 yr).

L7 ANSWER 29 OF 48 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

1982:189604 Document No.: PREV198273049588; BA73:49588. LIGNANS IN EASTERN HEMLOCK TSUGA-CANADENSIS. NAVAS S M [Reprint author]; OMORI S. DEP DE MADERAS, INST TECNOL DE COSTA RICA, APARTADO 159, CARTAGO, COSTA RICA AC. Bulletin of the Iwate University Forests, (1981) No. 12, pp. 29-89.
ISSN: 0286-4339. Language: ENGLISH.

AB Comparisons of the chloroform-soluble extract components of eastern hemlock using standards from combined column chromatography, TLC and reverse phase high-pressure liquid chromatography [HPLC] techniques indicated the presence of the lignans pinoresinol, pinoresinol methyl ether, pinoresinol dimethyl ether, syringaresinol, conidendrin, **matairesinol**, oxomatairesinol, **hydroxymatairesinol**, liovil and isolariciresinol. Only conidendrin had been previously reported in eastern hemlock (Erdtman, 1944). α- and β-Conidrendrol were not present in the heartwood chloroform-soluble extract. Although open column elution chromatography is a useful technique for the partial separation of natural mixtures of lignans, it is not adequate for the isolation of pure lignans. Silica gel or cellulose TLC was a good method for identification of lignans. The use of reverse phase HPLC in the analysis of lignans was not previously reported. Reverse phase HPLC is a sensitive and rapid method for the separation of lignans. Pinoresinol and conidendrin, e.g., were separable by reverse phase HPLC but were not readily separable by silica gel TLC. There were instances in which the technique could not distinguish between separate lignans. The following pairs of standards could not be separated: liovil

and and **hydroxymatairesinol**, α-conidendrin and **matairesinol**, and pinoresinol and syringaresinol. The system was inadequate for the separation of liovil, **hydroxymatairesinol** and isolarioiresinol in natural mixtures. The reverse phase HPLC method is both rapid and relatively easy to use. Most of the peaks of the chromatograms were produced within 15 min of injection of the lignan-containing samples. The preparation of derivatives was unnecessary since pure compounds or mixtures can be injected into the chromatograph in their natural state.

L7 ANSWER 30 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
1982:102368 Document No. 96:102368 Lignane in oak wood and cognac alcohols. Kuridze, M. G.; Mudzhiri, L. A.; Lashkhi, A. D.; Leont'eva, V. G.; Semenov, A. A. (Nauchno-Issled. Inst. Sadovod. Vinograd. Vinodel., Tbilisi, USSR). Vinodelie i Vinogradarstvo SSSR (8), 12-14 (Russian) 1981. CODEN: VIVSA6. ISSN: 0042-6318.
AB A method is described for determining lignin substances in oak wood and cognac, based on extraction with organic solvents (acetone, CHCl3-MeOH, C6H6-EtOAc, and CHCl3-acetone), followed by TLC on silica gel and spectrophotometry. Nine lignin substances were identified: secoisolariciresinol [29388-59-8], liovil [484-39-9], lariciresinol [27003-73-2], olivil [2955-23-9], pinoresinol [487-36-5], eudesmin [526-06-7], **matairesinol** [580-72-3], **hydroxymatairesinol** [20268-71-7], and isolariciresinol [548-29-8]. The contents of each of these substances in wine increased significantly upon prolonged storage from 4.5 mg/mL (after 1 yr) to 16 mg/mL (after 20 yr).

L7 ANSWER 31 OF 48 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN
1978:192745 Document No.: PREV197866005242; BA66:5242. O ACYL DERIVATIVE LIGNANS FROM WOOD OF THE GENUS ABIES. LEONT'EVA V G [Reprint author]; MODONOVA L D; TYUKAVKINA N A; PUNTUSOVA E G. IRKUTSK INST ORG CHEM, SIB DEP, ACAD SCI USSR, IRKUTSK, USSR. Khimiya Prirodnykh Soedinenii, (1977) No. 3, pp. 337-341.
CODEN: KPSUAR. ISSN: 0023-1150. Language: RUSSIAN.
AB Five new compounds were chromatographically isolated from the wood of A. sibirica and A. nephrolepis. These proved to be complex esters derivatives of the lignans lariciresinol, olivil and **hydroxymatairesinol.** Their structure was analyzed on the basis of spectroscopic data.

L7 ANSWER 32 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
1978:71443 Document No. 88:71443 Lignan compounds in the needles of some species of the Pinaceae family. Tyukavkina, N. A.; Medvedeva, S. A.; Ivanova, S. Z.; Lutskii, V. I. (Inst. Org. Khim., Irkutsk, USSR). Koksnes Kimija (6), 94-6 (Russian) 1977. CODEN: KHDRDQ. ISSN: 0201-7474.
AB Of the lignans extracted from needles of fir, spruce, larch, and pine species, secoisolariciresinol was present in all species, except those of fir; liovil, lariciresinol, **matairesinol**, and isolariciresinol were found in all species, olivil was absent in fir species, Picea ajanensis, and Larix sibirica; pinoresinol was absent in Abies sibirica and L. sibirica; **hydroxymatairesinol** was found only in spruce species; ketomatairesinol trace amts. were detected in P. koreansis only; and α-conidendrin was found in trace amts. in L. dahurica only. The total lignan content of needles was 0.03-0.09% (on dry-weight basis). The needles did not contain 3,4-divanillyltetrahydrofuran, which is normally present in wood.

L7 ANSWER 33 OF 48 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN DUPLICATE 9
1977:221829 Document No.: PREV197764044193; BA64:44193. DISTRIBUTION AND PHENOLIC COMPOSITION OF SAP WOOD AND HEART WOOD IN ABIES-GRANDIS AND EFFECTS OF THE BALSAM WOOLLY APHID. PURITCH G S. Canadian Journal of Forest Research, (1977) Vol. 7, No. 1, pp. 54-62.
CODEN: CJFRAR. ISSN: 0045-5067. Language: Unavailable.

AB The distribution of sapwood and heartwood was analyzed at 3 different height levels in A. grandis (Dougl.) Lindl infested and non-infested with balsam woolly aphid [Adelges piceae (Ratz.)]. In non-infested trees, there was a highly significant regression between percentage heartwood age and disk age and a less significant regression between percentage heartwood area and disk area. Aphid infestation increased both the number of annual rings of heartwood and the heartwood area. The amount of heartwood in the infested trees was highly variable and dependent upon the degree of aphid infestation. Phenolic composition of A. grandis was similar to western hemlock [Tsuga heterophylla (Raf.) Sarg.] with heartwood containing **matairesinol**, **hydroxymatairesinol**, conidendrin and an unknown phenolic glucoside. Sapwood contained several leucoanthocyanidins. Aphid infestation did not alter the phenolic composition of the heartwood, but it did cause the occurrence of a new phenolic in the sapwood. The possible causes of the increased amounts of heartwood in infested trees are discussed.

L7 ANSWER 34 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
1976:474919 Document No. 85:74919 Analysis of lignans in Norway Spruce by combined gas chromatography-mass spectrometry. Ekman, Rainer (Inst. Wood Chem. Cellul. Technol., Abo Akad., Abo, Finland). Holzforschung, 30(3), 79-85 (English) 1976. CODEN: HOLZAZ. ISSN: 0018-3830.
AB Me2CO-soluble lignans of spruce wood contained 0.5% guiaiacyl type lignans. The compds. identified in the extract were isolariciresinol, secoisolariciresinol, liovil, α-conidendric acid, lignan A and B, lariciresinol, 2 **hydroxymatairesinol** isomers, pinoresinol, **matairesinol**, and α-conidendrin. Six unidentified lignans of the tetrahydrofuran series were also detected.

L7 ANSWER 35 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
1974:532858 Document No. 81:132858 Lignans from Picea koraiensis wood. Leont'eva, V. G.; Modonova, L. D.; Tyukavkina, N. A. (Irkutsk. Inst. Org. Khim., Irkutsk, USSR). Khimiya Prirodnykh Soedinenii (3), 399-400 (Russian) 1974. CODEN: KPSUAR. ISSN: 0023-1150.
AB Lignan contents (3,4-divanillyltetrahydrofuran, liovil, lariciresinol, pinoresinol, ketomatairesinol, **matairesinol**, **hydroxymatairesinol**, isolariciresinol, α-conidendrin, and vanillin) in P. koraiensis, P. obovata, and P. ajanensis are tabulated. P. ajanensis contained more cyclic lignans than the other 2.

L7 ANSWER 36 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
1974:548518 Document No. 81:148518 Lignans from Abies sibirica wood. Leont'eva, V. G.; Modonova, L. D.; Tyukavkina, N. A. (Irkutsk. Inst. Org. Khim., Irkutsk, USSR). Izvestiya Sibirskogo Otdeleniya Akademii Nauk SSSR, Seriya Khimicheskikh Nauk (4), 158-61 (Russian) 1974. CODEN: IZSKAB. ISSN: 0002-3426.
AB The acetonic extract fraction insol. in ligroin contained secoisolariciresinol (I), 3,4-divanillyltetrahydrofuran (II), liovil (III), lariciresinol (IV), pinoresinol (V), olivil, **matairesinol**, and **hydroxymatairesinol**. Of these, I-V were determined for the 1st time in the wood of the Abies genus.

L7 ANSWER 37 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
1975:141811 Document No. 82:141811 Lignan compounds of Siberian spruce wood (Picea obovata). Modonova, L. D.; Tyukavkina, N. A. (Irkutsk. Inst. Org. Khim., Irkutsk, USSR). Khim. Ispol'z. Lignina, 73-86. Editor(s): Sergeev, V. N. "Zinatne": Riga, USSR. (Russian) 1974. CODEN: 29THA7.
AB The extraction of Picea obovata with MeOH or acetone gave 8.8 or 8.7% (on dry wood weight) resp. of phenolic constituents. These compds. were separated by thin layer chromatog. and identified as conidendrin [518-55-8], 3,4-divanillyltetrahydrofuran [34730-78-4], pinoresinol [487-36-5], **matairesinol** [580-72-3], ketomatairesinol [53250-61-6], lariciresinol [27003-73-2], **hydroxymatairesinol** [20268-71-7], and liovil [484-39-9]. The wood of Picea obovata had low resistance to fungus infection. Biol. testing showed that none of the above-indicated

lignans had any fungicidal properties.

L7 ANSWER 38 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
1975:74652 Document No. 82:74652 Lignans from Abies nephrolepis and Picea ajanensis. Leont'eva, V. G.; Modonova, L. D.; Tyukovkina, N. A. (Irkutsk. Inst. Org. Khim., Irkutsk, USSR). Khimiya Prirodnykh Soedinenii (2), 268-9 (Russian) 1973. CODEN: KPSUAR. ISSN: 0023-1150.
AB The phenolic substances, extracted from Picea ajanensis with acetone, include α-conidendrin [518-55-8], **matairesinol** (I) [580-72-3], ketomatairesinol, **hydroxymatairesinol** (II) 3,4-divinyltetrahydrofuran (III) [41233-91-4], (+)-pinoresinol (IV) [487-36-5], liovil (V) [484-39-9], isolariciresinol [548-29-8], vanillin (VI) [121-33-5], and vanillic acid [121-34-6]. The exts. from Abies nephrolepis contain I-VI. The substances were separated by chromatog. on powdered polyamide and silica gel impregnated with 2% Na metabisulfite solution

L7 ANSWER 39 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
1973:99363 Document No. 78:99363 Isolation of two lignans from Ezomatsu (Picea jezoensis). Omori, Shigetoshi; Sakakibara, Akira (Fac. Agric., Hokkaido Univ., Sapporo, Japan). Mokuzai Gakkaishi, 19(1), 41-4 (Japanese) 1973. CODEN: MKZGA7. ISSN: 0021-4795.
AB The title wood meal was extracted with 1:2 EtOH-benzene, concentrated, and extracted with petroleum ether to give (-)-α-conidendrin (I) [518-55-8] and (-)-**hydroxymatairesinol** (II).

L7 ANSWER 40 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
1971:506237 Document No. 75:106237 Phenolic extractives in Norway spruce and their effects on Fomes annosus. Shain, Louis; Hillis, W. E. (Div. Forest Prod., CSIRO, South Melbourne, Australia). Phytopathology, 61(7), 841-5 (English) 1971. CODEN: PHYTAJ. ISSN: 0031-949X.
GI For diagram(s), see printed CA Issue.
AB **Hydroxymatairesinol** (I), **matairesinol**, liovil, and conidendrin were identified in healthy heartwood tissue of Norway spruce (Picea abies) as well as in the reaction zone separating healthy sapwood from wood decayed by F. annosus. The reaction zone contained considerably more I than was found in heartwood. Healthy sapwood and wood in advanced stages of decay contained negligible quantities of lignans. I was significantly more inhibitory to F. annosus than was matariresinol or conidendrin in vitro. I in association with the alkalinity in the reaction zone may contribute to the resistance of the sapwood to F. annosus in vivo.

L7 ANSWER 41 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
1971:1050 Document No. 74:1050 Oxy- and keto-**matairesinols** from Picea obovata. Modonova, L. D.; Leont'eva, V. G.; Tyukavkina, N. A. (Irkutsk. Inst. Org. Khim., Irkutsk, USSR). Khimiya Prirodnykh Soedinenii, 6(4), 477 (Russian) 1970. CODEN: KPSUAR. ISSN: 0023-1150.
AB Hydroxy- and ketomatairesinols were isolated from the wood of P. obovata.

L7 ANSWER 42 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
1970:511114 Document No. 73:111114 Cellular distribution of lignans in Tsuga heterophylla wood. Krahmer, R. L.; Hemingway, R. W.; Hillis, W. E. (Forest Prod. Lab., C.S.I.R.O., South Melbourne, Australia). Wood Science and Technology, 4(2), 122-39 (English) 1970. CODEN: WOSTBE. ISSN: 0043-7719.
AB Western hemlock heartwood contained tracheids with large amts. of cellular inclusions and deposits containing the lignans **matairesinol**, **hydroxymatairesinol**, and conidendrin. The deposits occurred in 3 different forms and various chemical compns. Rays contained deposits phys. similar to those in adjacent tracheids, but did not contain lignans, although lignans were present in the tracheids. Lignans formed surface films on tracheid walls and encrusted the bordered pits. The amount of lignans was not related to wet wood zones. The lignan biosynthesis probably occurred in the heartwood periphery in the vicinity of the

half-bordered pits.

L7 ANSWER 43 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
1968:115792 Document No. 68:115792 Significance of western hemlock phenolic extractives in pulping and lumber. Barton, George M. (Forest Prod. Lab., Vancouver, BC, Can.). Forest Products Journal, 18(5), 76-80 (English) 1968. CODEN: FPJOAB. ISSN: 0015-7473.
AB Western hemlock wood contains a great variety of phenolics ranging from simple monomers to lignin dimers, which could result in either utilization problems or potential silivichemicals. The more important phenolics isolated from western hemlock are α-conidendrin (I), **hydroxymatairesinol** (II), **matairesinol** (III), leucocyanidin (IV), and catechin (V). Recently guaiacylglycerol (VI) and 2-(α-hydroxyguaiacyl)-5-(3-hydroxypropyl)-7-methoxycoumarin (VII) were discovered in hemlock sapwood. Some of the extractives are reviewed briefly and the brown stains on sapwood lumber and the low brightness of groundwood pulp are discussed in detail. The sapwood contains 3 IV, V, VI, and VII. The heartwood exts. contain I, II, and III. There is also a large transition zone between inner heartwood and outer sapwood containing extractives common to both. Only I has been produced in com. amts. V is suspected in the low brightness of hemlock groundwood pulp.

L7 ANSWER 44 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
1963:464128 Document No. 59:64128 Original Reference No. 59:11887e Conidendrin in floccosoids of western hemlock. Barton, G. M. (Forest Prods. Res. Branch, Vancouver, Can.). Forest Prod. J., 13, 304 (Unavailable) 1963.
AB White flecks (floccosoids) occasionally found in western hemlock (Tsuga heterophylla) were isolated and shown to be identical with conidendrin. **Hydroxymatairesinol** is probably its precursor.

L7 ANSWER 45 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
1962:79188 Document No. 56:79188 Original Reference No. 56:15394h-i,15395a-c Occurrence of **matairesinol** in mountain hemlock (Tsuga mertensiana), Western Hemlock (Tsuga heterophylla), and balsam (Abies amabilis). Barton, G. M.; Gardner, J. A. F. (Dept. Forestry Can., Vancouver). Journal of Organic Chemistry, 27, 322-3 (Unavailable) 1962. CODEN: JOCEAH. ISSN: 0022-3263.
AB Heartwood (100 g.) of the 3 species macerated with MeOH and the thin slurry filtered, the filtrate evaporated at 50° in vacuo in a tared flask and the flask and contents degassed 2 hrs. at 20° under high vacuum, weighed and adjusted with MeOH to 25 mg./ml. Two dimensional chromatograms using 60:25:15 BuOH-H2O-AcOH against the machine direction and 2% AcOH in the machine direction were run on Whatman Number 1 for 8 hrs. and 1.5 to 2.0 hrs. in the resp. solvents. The spots were detected by ultraviolet light and a series of agents including diazotized H2NC6H4SO3H. **Matairesinol** (I) and conidendrin (II) were detected in all exts. The reversed phase system of Freudenberg and Knof (CA 52, 15494c) using filter paper strips saturated with HCONH2 and run upwards with MeCH(OEt)2 saturated with HCONH2 gave a vivid red-purple spot (diazotized p-H2NC6H4SO3H) at Rf 0.21 corresponding to I with all 3 exts. II (Rf 0.15), **hydroxymatairesinol** (Rf 0.05) and unidentified components were also present. I, m. 119°, from mountain hemlock had λmaximum 231, 282 mμ (log ε 4.13, 3.84), λmin. 231 mμ (log ε 4.13), similar to values given by a reference sample, ν 3400, 2925, 2000, 1870, 1770, 1610, 1520, 1460, 1440, 1380, 1355, 1272, 1240, 1208, 1150, 1125, 1080, 1020, 965, 940, 922,890, 870, 850, 830, 792, 782, 750, 720,680, 650 cm.-1 [lower-melting material, m. 66-7° (alc.), had a similar spectrum with broad peaks at I725-60 and 1360-80 cm.-1 (KBr)], [α]25D -45° (c 2%, Me2CO), with [α]25D -42.2°, for lower-melting material. In tests cooks with aqueous NaHSO3 and NaHSO3-SO2, unchanged I was recovered. Waste sulfite liquor extract contained I and II. I occurs also in heartwood extract of Abies grandis and its occurrence in A. concolor and A. procera may be expected

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1962:67776 Document No. 56:67776 Original Reference No. 56:13131i,13132a-c
Examination of western hemlock for lignin precursors. Goldschmid, Otto; Hergert, H. L. (Rayonier, Inc., Shelton, WA). Tappi, 44, 858-70 (Unavailable) 1961. CODEN: TAPPAP. ISSN: 0039-8241.

AB The cambium and sapwood of western hemlock (Tsuga heterophylla) were examined for the presence of low-mol.-weight components which might be intermediates in lignin formation. This knowledge would provide further information on the structure of lignin. The following extractive substances were detected in the cambium: quinic acid (I), shikimic acid (II), sucrose, fructose, arabogalactan, coniferin, leucocyanidin, catechol (III), epicatechol, and depsides of the following acids: caffeic-shikimic, ferulic-shikimic, ferulic-quinic, and p-coumaric-shikimic. A 5th depside was tentatively identified as p-coumaryl-quinic acid. In addition to these compds., several glycosides of lignanlike compds. were detected, but their structure has not yet been completely elucidated. The following compds. were isolated from, or detected in, the sapwood: Brauns' "native lignin," conidendrin, **hydroxymatairesinol**, oxomatairesinol, pinoresinol, dehydrodiconiferyl alc., vanillic acid, vanillin, coniferylaldehyde, ferulic acid, fumaric acid, sequoyitol, pinitol, I, II, III, leucocyanidin, xylose, arabinose, mannose, glucose, galactose, rhamnose, and several incompletely characterized lignin glycosides. The presence of guaiacylglycerol β-coniferyl ether was indicated but not definitely ascertained. Depsides were absent. The presence in the cambium of phenolic glucosides and the absence of Freudenberg's proposed intermediates in lignin formation indicate that either these intermediates are of such a transitory nature that they cannot be detected, or that lignin formation proceeds via glucoside intermediates. Not directly related, but of interest, was the observation that conidendrin is formed during sulfite cooking by dehydration of **hydroxymatairesinol.**

L7 ANSWER 47 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN
1958:88001 Document No. 52:88001 Original Reference No. 52:15494c-i,15495a-i,15496a-c The lignans of fir wood. Freudenberg, Karl; Knof, Leo (Univ. Heidelberg, Germany). Chemische Berichte, 90, 2957-69 (Unavailable) 1957. CODEN: CHBEAM. ISSN: 0009-2940.

AB A 20-30 years old fir freed of its bark and dried, resin-free pieces reduced to saw dust, 4-kg. portions air-dried saw dust each in three 16-1. percolators extracted with 85% aqueous Me2CO, the 1st 20 l. percolate from the 1st percolator passed through the 2nd and 3rd percolator during 10 days, the percolate from a total of 40 kg. wood evaporated in vacuo, the tacky residue (637 g.) added to 400 cc. anhydrous Me2CO, the resulting 2 phases centrifuged from a small amount of solid, the 2-phase supernatant evaporated in vacuo, a 100-g. portions of the solid residue dissolved in 100 cc. 4:1 HCONH2-H2O, the solution washed with three 60-cc. portions Et2O, and the Et2O washing and the aqueous solution subjected to a countercurrent distribution with
1:3 HCONH2-H2O (saturated with Et2O) yielded the following fractions (designation of fraction, tube number, color of coupling product with diazotized sulfanilic acid in 2% aqueous Na2CO3, % of charge, and main components given): A, up to 238, almost none, 29.3, phenol-free material; B, 239-660, red, 9.5, red-coupling lignans; C, 661-1278, yellow, 16.2, **hydroxymatairesinols**; D, 1279-2100, yellow, 3.6, liovil (I); E, 2101-2380 and 120-200, yellow, 2.5, yellow-coupling substances; F, 70-119, yellow, 1.7, yellow-coupling substances; G, 35-69, yellow, 3.3, yellow-coupling substances; H, 1-34, yellow, 9.6, dissolved lignin portion; I, 1-34, yellow, 20.3, undissolved lignin portion. The phenol free resin fraction A (60 g.) distilled at 0.4 mm. to 300° gave 35 g. distillate which redistd. yielded 14 g. distillate, b0.01 to 180°, and 15 g. distillate, b0.01 180-98°. The first distillate fraction hydrogenated gave 4.5 g. stearic acid. Fraction B (37 g.) gave after removal of the Et2O 5 g. crystalline (-)-α-conidendrin (II), m. 238° with resolidification and rem. 256° (HCO2H and EtOH), [α]25D -71.4° (c 4, tetrahydrofuran), -54.5° (Me2CO); II freshly recrystd. from HCO2H showed sometimes a m.p. of 242-3°

with resolidiflcation and rem. 262-3°. The mother liquor from the II evaporated, the residue dissolved in tetrahydrofuran, the solution evaporated, the residue (31 g.) redissolved in 80 cc. HCONH2, and the solution subjected to a countercurrent distribution with 1:1 HCONH2-H2O (saturated with Et2O) yielded the following fractions (same data given): B-1, to 347, almost none, 6, phenol-free materials; B-2, 348-447, lemon-yellow with blue fluorescence, 7, coniferylaldehyde (III) with little 3,4-divanillyltetrahydrofuran (IV) and vanillin (V); B-3, 448-687, red, 21, pinoresinol (VI) and **matairesinol** (VII); B-4, 688-1005, gray-red, 20, II with a little VII; B-5, 1000-1349, red-violet, 14, oxomatairesinol (VIII) and II; B-6, 1350-1728, red, 9, lariciresinol (IX) with a little II; B-7, 1729-1915 and 160-200, red, 4, II with a little **hydroxymatairesinols**; B-8, 100-159, yellow, 7, **hydroxymatairesinols**; B-9, 1-99, yellow, 2, -. Fraction B-2 in EtOH treated with KOAc in EtOH, the adduct treated with H2O containing a small amount of hydroquinone and filtered, and the residue dried and recrystd. from C6H6 containing a trace of hydroquinone gave III; 2,4-dinitrophenylhydrazone, m. 266-9°. The filtrate from the adduct evaporated, the residue treated with CH2Cl2 and H2O, the organic layer evaporated, and the residue dissolved in EtOH and treated with 3 g. 2,4-(O2N)2C6H3NHNH2 in 100 cc. EtOH and 2 cc. concentrated HCl gave the 2,4-dinitrophenylhydrazone of V, m. 266-7°. The presence of IV in fraction B-2 was demonstrated by the paper chromatogram. Fraction B-3 (3.5 g.) ground with 6 cc. saturated alc. KOAc, allowed to stand 6 hrs., and filtered, and the residue washed with alc. KOAc and decomposed with CH2Cl2 and H2O yielded 1.4 g. (crude) (+)-VI, m. 119-20° (EtOH), containing 13% (±)-VI, which recrystd. further gave 94%-pure (+)-VI, [α]21D 84.4° (c 5, Me2CO). Fraction B-3 (4 g.) combined with 2 g. residue from the isolation of the VI and dissolved in 50 cc. CHCl3, and the solution subjected to a 495-transfer countercurrent distribution yielded in the tubes 142-192 1.26 g. (crude) (-)-VII, m. 116-18° (30% aqueous AcOH), [α]25D -45.0° (c 4.2, Me2CO); di-Me ether, m. 129-30°, [α]25D -31.8° (c 1.7, CHCl3). Fraction B-4 digested with a little AmOH and filtered gave II. Fraction B-5 (4 g.) in 25 cc. CHCl3 subjected to a 375-transfer countercurrent distribution with 3:2.5:6 HCONH2-H2OCHCl3 yielded in tubes 80-118 2 g. (+)-VIII, m. 70-2°, [α]25D 42.6° (c 4.0, tetrahydrofuran) (diacetate, needles, m. 122-3° (EtOH)], and in tubes 20-42 0.8 g. II. VIII in EtOAc hydrogenated in the presence of PdCl2 yielded VII, m. 116-17°, [α]25D -45.1° (c Me2CO). VIII in EtOAc hydrogenated 2 days over 5% Pd-kieselguhr gave in addition to VII and VIII also (-)-**hydroxymatairesinol** (X), and (-)-allohydroxymatairesinol (XI); the crude product treated with alc. KOAc gave the X-KOAc adduct, m. 120-2°. Fraction B-6 crystallized partially to deposit IX. The combined fractions C and B-8 (10 g.)in 15 cc. HCONH2 and 3 cc. H2O subjected to a 2630-transfer countercurrent distribution with 1:3.5:5 HCONH2-H2O-CHCl3 gave 2.7 g.-amorphous X, [α]22D -11.0° (c 4.0, tetrahydrofuran), -6.3° (c 4, EtOH), and 4.0 g. XI, [α]25D -9.8° (c 4.0, tetrahydrofuran), 4.9° (c 4, EtOH). A mixture (10 g.) of X and XI kept 1 day at 20° with 10 cc. saturated alc. KOAc and filtered, and the residue washed with a little PrOH yielded 6.5 g. X-KOAc adduct, m. 126-7° (BuOH). X gave also with PrOH saturated with EtCO2K a crystalline adduct. X-KOAc adduct (6 g.) dissolved in a few cc. 2:3 Me2CO-H2O, shaken with 70 cc. H2O and 75 cc. CH2Cl2, the aqueous layer extracted with CH2Cl2, and the combined CH2Cl2 solns. evaporated while protected from light gave 4.4 g. colorless residue; X-XI mixture heated with alc. KOAc yielded with the disappearance of the X-XI apparently higher mol. weight orange-yellow coupling material. X (1 g.) dissolved in 60° in 1 g. NaOH in 1 cc. H2O, cooled, neutralized with 50% AcOH, cooled with ice, and filtered, the residue washed with dilute aqueous NaOAc, dissolved in 10 cc. MeOH, and the solution diluted with 15 cc. C6H6 gave 0.3 g. Na (-)-hydroxymatairesinolate, prisms, which acidified with moderately dilute AcOH gave oily crystals. X with 2,4-(O2N)2C6H3F gave a yellow

amorphous powder which subjected to countercurrent distribution with 5:3.5:1.5, CH_2Cl_2-MeOH-H_2O, then with 3:2:1:0.6, and finally with 5:4.5:1.5:1 $HCONMe_2$-C_6H_6-cyclohexane-H_2O yielded the 2,4-dinitrophenyl ether derivative of X, amorphous solid; acetate, amorphous solid. X with CH_2N_2 gave the di-Me ether, m. 96-7° (AmOH), [α]25D 59.8° (c 2.0, tetrahydrofuran). X (0.5 g.) in EtOAc hydrogenated over 0.2 g. Pd during 16 hrs., filtered, and evaporated, and the residue recrystd. from 3:7 glacial AcOH-H_2O yielded 71% (-)-VII. XI gave similarly 50% (-)-VII. II converted to the di-Me ether and then treated with $Pb(OAc)_2$ gave a phenylnaphthalene derivative, m. 216-17° with resolidification and rem. 225-7°. X (0.20 g.) in 5 cc. of a solution of 1 cc. concentrated H_2SO_4 in 20 cc. tetrahydrofuran showed the following [α]25D values at the times in min. given in parentheses: -6.1° (10), 1.4° (35), 11.7° (105), 19.0° (260), 19.4° (290), 3.1° (1185), -1.7° (1415), -21.6° (2520), -42.4° (4140), -56.8° (5950), -58.0° (6000). This change of rotation indicates a conversion of X to II. Fraction D (3.5 g.) digested with 8 cc. AmOH, refrigerated 18 hrs., and filtered gave 0.8 g. (-)-I, prisms, m. 173.5-4.5° (aqueous MeOH), [α]25D -32.8° (c 4.0, MeOH); tetraacetate, m. 124-5° (EtOH). The AmOH extract from fraction D evaporated, the residue dissolved warm in 375 cc. $CHCl_3$ and 375 cc. H_2O, and the mixture subjected to a 185-transfer countercurrent distribution gave in tubes 90-125 an addnl. 0.36 g. (-)-I. (-)-I (0.25 g.) in EtOAc hydrogenated 2 days over 0.2 g. Pd black gave IV, prisms, m. 116-17° (Me_3COH), [α]25D -52.2° (c 1.4, tetrahydrofuran). VI in EtOAc hydrogenated 1.5 hrs. over prehydrogenated $PdCl_2$ and the mixture chromatographed on paper showed the presence of VI, IX, and 2,3-divanillyl-1,4-butanediol, Rf 0.85 ($HCONH_2$-Et_2O), which coupled with a red-violet color; the mixture dehydrated by the method of Haworth and Woodcock (C.A. 33, 68332) yielded 35% IV, m. 116-17°. (+)-IX hydrogenated in EtOAc in the usual manner yielded during 40 min. 70% IV, [α]25D -51.8° (c 4.0, tetrahydrofuran). IV showed the following Rf values with the listed solvents saturated with $HCONH_2$: Et_2O 0.67, $CHCl_3$ 0.91, $CHCl:CCl_2$ 0.67, PhCl 0.66, C_6H_6 0.61, CCl_4 0.35, cyclohexane 0.02. IX showed under the same conditions the following Rf values: Et_2O 0.14, $CHCl_3$ 0.38, PhCl 0.04, C_6H_6 0.03, CH_2Cl_2 0.34. IV showed the following Rf values with the listed solvents half-saturated with $HCONH_2$: $MECH(OMe)_2$ 0.68, $MeCH(OEt)_2$ 0.64. IX showed under the same conditions the following Rf values: $MeCH(OMe)_2$ 0.43, $MeCH(OEt)_2$ 0.18, CH_2Cl_2 0.41. The Rm values (cf. Brooks, et al., C.A. 51, 12113d) were determined for the following compds.: dehydrodiisoeugenol -0.85, dehydrodiconiferyl alc. 0.91, X 1.00, VII 0.25, I 1.28, IV -0.25, VIII 0.63, II 0.42. From these values were calculated the following Rf group increments: OH (γ) 0.88, OH (α) 0.75, OH (α) 0.76, α-oxo group 0.38, ring closure with the loss of 2H 0.17. The red coupling amorphous trace amts. (accompanying II in fraction B) with Rf 0.54-0.55 might possibly be 2,5-diguaiacyl-3,4-dimethyltetrahydrofuran for which an Rf value of 0.54 is calculated

L7 ANSWER 48 OF 48 CAPLUS COPYRIGHT 2004 ACS on STN

1957:32007 Document No. 51:32007 Original Reference No. 51:6145g-i,6146a-d

Application of radioactive isotopes to the elucidation of lignin. VI. The origin of the isohemipic acid. Freudenberg, Karl; Niedercorn, Francois (Univ. Heidelberg, Germany). Chemische Berichte, 89, 2168-73 (Unavailable) 1956. CODEN: CHBEAM. ISSN: 0009-2940.

AB cf. C.A. 49, 6598a. Artificial lignin, the dehydrogenation polymerizate (DHP) of coniferyl alc. (I), is prepared by 2 methods: the influx (Zulauf) and the dropping (Zutropf) method. In the former, the total I is available to the enzyme in one batch, whereas in the latter, I is available to the enzyme in a very dilute state at the rate at which it is consumed. In both cases, dehydrodiconiferyl alc. (II), DL-pinoresinol (III), and guaiacyl-glycerol coniferyl ether (IV) are formed in about 80% yield, with IV predominating in the dropping method. The residual 20% seems also to be chiefly dimeric compds. I-IV have also been found in the cambial sap. The soluble lignin contains **matairesinol**,

conidendrin, and a compound which may be **hydroxymatairesinol.** However, there is present in lignin some combination of building stones which must explain the formation of isohemipic acid (V) from sprucewood after methylation with CH2N2 without previous alkali treatment, and the formation of dehydrodivanillin as found by Pew (C.A. 50, 3422h.) on oxidation of lignin with PhNO2 and alkali. The difference in phenolic OH as determined by optical and titration methods cannot be explained by the secondary lignin building stones, I-IV. To study the origin of the C atom of the CO2H group at the 5-position in V, I labeled with C14 at the β-C atom of the side chain has been prepared and converted into the DHP. Acetylvanillin (450 mg.), 185 mg. C14H2(CO2H)2 (2 + 107 impulses/millimole/min.), 2 cc. C5H5N, and 2 drops PhNH2 are heated 8 hrs. at 60° and yield 90% acetylferulic acid which is heated with 2 cc. SOCl2, 1 drop C5H5N, and 5 cc. C6H6 2 hrs. at 75°. The solution is evaporated in vacuo, giving 370 mg. acetylferulic acid chloride, m. 147-9°. This is treated in 5 cc. C6H6 and 30 cc. tetrahydrofuran (THF) 24 hrs. with 120 mg. LiA1H4 in 30 cc. THF, the precipitate decomposed with 22 mg. (NH4)2CO3 in 10 cc. H2O and a trace of Na dithionite, extracted with Et2O, and the residue of the Et2O recrystd. from CH2Cl2-petr. ether, giving 81% radioactive, I, m. 72°. Inactive I (7 g.) and 150 mg. active I in 51. H2O and 1 l. phosphate buffer of pH 7 in the presence of 350 mg. mushroom dehydrase are treated with O 5 days at 15°, the precipitated DHP is centrifuged, washed with H2O, dissolved in Me2CO, and precipitated with C6H6, giving 5.6 g. radioactive DHP (VI) with a sp. activity of 402,000 impulses/millimole/min. (calculated on the basis of an equivalent of 188). Treatment of 2 g. DHP with KOH, methylation, and oxidation with KMnO4 give 53 mg. active V, m. 245°, with a sp. activity of 385,000 impulses/millimole/min. The simultaneously formed veratric acid is inactive. Methylation of 1.5 g. VI with CH2N2 and oxidation with KMnO4 at pH 7 yield 0.9% active V, with 382,000 impulses/millimole/min. Refluxing 2.5 g. VI 10 hrs. in 25 cc. MeOH and 3 cc. concentrated HCl, evapg, the solution, methylating the residue with Me2SO4-NaOH, and oxidizing the product with KMnO4 give 21 mg. m-hemipic acid (VII), m. 174°, with only a trace of radioactivity. Distilling 500 mg. VI with 28% H2SO4 yields practically inactive HCHO. For the chromatographic separation of the acids a mixture of BuOHH2O-morpholine (100:15:10) is used, giving the following Rf values: for veratric acid 0.65, VII 0.35, V 0.25, and dehydrodiveratric acid 0.10.

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=> s (eriksson j?/au or kangas l?/au or komi j?/au or perala m?/au or korte h?/au)
L8         3504 (ERIKSSON J?/AU OR KANGAS L?/AU OR KOMI J?/AU OR PERALA M?/AU
                OR KORTE H?/AU)

=> s l8 and hydroxymatairesinol
L9           21 L8 AND HYDROXYMATAIRESINOL

=> dup remove l9
PROCESSING COMPLETED FOR L9
L10          11 DUP REMOVE L9 (10 DUPLICATES REMOVED)

=> d l10 1-11 cbib abs

L10  ANSWER 1 OF 11  BIOSIS  COPYRIGHT (c) 2004 The Thomson Corporation.  on
     STN
2004:181735  Document No.: PREV200400185021. Food additive or product or a
     pharmaceutical preparation, comprising hydroxymatairesinol.
     Ahotupa, Markku [Inventor, Reprint Author]; Eckerman, Christer [Inventor];
     Kangas, Lauri [Inventor]; Makela, Sari [Inventor]; Saarinen, Niina
     [Inventor]; Santti, Risto [Inventor]; Warri, Anni [Inventor]. Turku,
     Finland. ASSIGNEE: Hormos Nutraceutical Oy Ltd., Turku, Finland. Patent
     Info.: US 6689809 February 10, 2004. Official Gazette of the United States
     Patent and Trademark Office Patents, (Feb 10 2004) Vol. 1279, No. 2.
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http://www.uspto.gov/web/menu/patdata.html. e-file.
ISSN: 0098-1133 (ISSN print). Language: English.

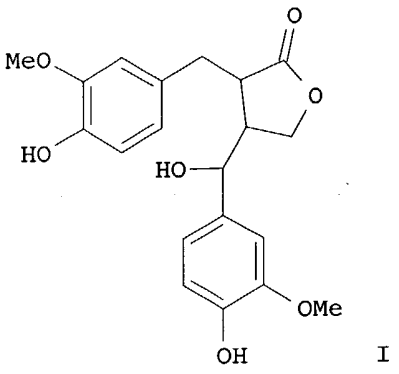
AB This invention relates to methods for prevention of cancers, certain non-cancer, hormone dependent diseases and/or cardiovascular diseases in a person, based on administering of **hydroxymatairesinol** to said person. The invention also concerns a method for increasing the level of enterolactone or another metabolite of **hydroxymatairesinol** in a person's serum thereby causing prevention of a cancer or a certain non-cancer, hormone dependent disease in a person, based on administering of **hydroxymatairesinol** to said person. Furthermore, this invention relates to pharmaceutical preparations, food additives and food products comprising **hydroxymatairesinol.**

L10 ANSWER 2 OF 11 MEDLINE on STN DUPLICATE 1
2004363179. PubMed ID: 15265601. Prenatal developmental toxicity study with 7-**hydroxymatairesinol** potassium acetate (HMRlignan) in rats. Wolterbeek A P M; Roberts A; **Korte H**; Unkila M; Waalkens-Berendsen D H. (TNO Nutrition and Food Research, Toxicology and Applied Pharmacology Department, Zeist, The Netherlands.. wolterbeek@voeding.tno.nl) . Regulatory toxicology and pharmacology : RTP, (2004 Aug) 40 (1) 1-8. Journal code: 8214983. ISSN: 0273-2300. Pub. country: United States. Language: English.

AB Plant lignan 7-hydromatairesinol, a novel precursor of the mammalian lignan enterolactone was evaluated in a prenatal developmental toxicity study conducted in the Wistar rat. Mated female rats were fed diets containing 0, 0.25, 1, and 4% (w/w) of 7-**hydroxymatairesinol** in the form of potassium acetate complex (HMRlignan; potassium acetate level approximately 20% w/w within the preparation) for days 0-21 of gestation. Test substance intake was calculated to be 0.14-0.18, 0.46-0.74, and 1.19-2.93 g/kg body weight/day for the low, mid, and high-dose groups, respectively. The rats were sacrificed on day 21 of the gestation period and examined for standard parameters of reproductive performance (fecundity index, gestation index, number of corpora lutea, number of implantations, pre- and post-implantation loss, number of early- and late resorptions, number of live- and dead fetuses, sex-ration and the weight of the reproductive organs). The fetuses were examined for external, visceral, and skeletal alterations. The results from this study showed no effects on reproductive performance or any treatment related findings following external, visceral, and skeletal examination of the fetuses. However, approximately half of the mated dams of the high-dose failed to thrive due to an unexpected large decrease in their food intake, and were sacrificed early. Body weights of the remaining animals of the high-dose group were decreased. Food consumption was decreased in all treatment groups during the first three days of the gestation period as a result of decreased palatability of the feed. In conclusion, the no-observed-effect level (NOEL) for maternal effects was 1%, whereas the NOEL for fetal development following daily oral HMRlignan administration throughout the gestation was equivalent to 4% in the diet.

L10 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
2004:2687 Document No. 140:65203 Lignan topical formulations. **Korte, Helena**; Lehtola, Veli-Matti; Unkila, Mikko; Hiilovaara-Teijo, Mervi; Ahotupa, Markku (Hormos Nutraceutical Oy Ltd., Finland). PCT Int. Appl. WO 2004000304 A1 20031231, 25 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-FI375 20030515. PRIORITY: FI 2002-1184 20020619.

GI

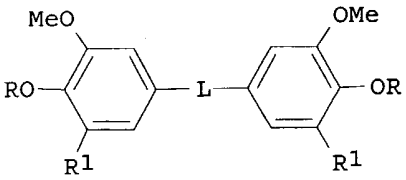


I

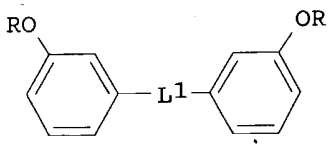
AB This invention concerns a topical formulation comprising a lignan or lignan ester in a dermatol. acceptable vehicle. The formulation can be either a cosmetic formulation or a pharmaceutical formulation. E.g., water-in-oil emulsions contained a lignan such as **hydroxymatairesinol** (I) or matairesinol dibutyrate, an emulsifier such as sorbitan fatty acid ester, humectant such as glycerol, preservative, and water.

L10 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
2003:633624 Document No. 139:179926 Preparation of lignan ester derivatives for use in pharmaceutical compositions and dietary supplements. Eklund, Patrik; Hiilovaara-Teijo, Mervi; Kalapudas, Arja; **Kangas, Lauri**; Lindholm, Anna; Sjoeholm, Rainer; Soedervall, Marja; Unkila, Mikko (Hormos Nutraceutical Oy Ltd., Finland). PCT Int. Appl. WO 2003066556 A1 20030814, 35 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2003-FI41 20030121. PRIORITY: FI 2002-222 20020205; FI 2002-563 20020325.

GI



I



II

AB The invention relates to novel phenolic esters of lignans I (R = COR', SO2R'; R1 = H, OMe; R' = (un)substituted C1-22-alkyl, alkenyl, arylalkyl, aralkenyl, aromatic (substituted with OH, carboxyl, oxo, amino); L = skeleton of **hydroxymatairesinol**, matairesinol, lariciresinol, secoisolariciresinol, isolariciresinol, oxomatairesinol, α-conidendrin, pinoresinol, liovil, picearesinol, arctigenin, syringaresinol, nortrachelogenin) and II (L1 = enterodiol, R ≠ Ac, COEt; L1 = enterolactone), their geometric or stereoisomers. Thus, matairesinol dibutyrate was prepared from matairesinol via acylation with EtCOCl in CH2Cl2 containing pyridine. Furthermore, the invention concerns pharmaceutical compns., dietary supplements, and food products comprising said esters.

L10 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
2003:417736 Document No. 138:406963 Method for the production of a phenolic substance from wood. Parhi, Seppo; Puska, Mervi; Kalapudas, Arja; **Korte, Helena**; Hukka, Petri (Hormos Nutraceutical Oy Ltd., Finland). PCT Int. Appl. WO 2003044004 A1 20030530, 14 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-FI905 20021115. PRIORITY: FI 2001-2290 20011123.

AB This invention concerns a method for the production of **hydroxymatairesinol** or a **hydroxymatairesinol** complex from wood comprising the steps of (a) extracting finely divided wood material with a polar solvent, (b) optionally concentrating the extract by separating at least part of the solvent. The invention is characterized by the steps of, (c) adding to the extract an agent able to form a complex with **hydroxymatairesinol**, and, (d) precipitating the **hydroxymatairesinol** complex, and optionally, (e) releasing the **hydroxymatairesinol** from the complex.

L10 ANSWER 6 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
2003:414080 Document No. 138:379228 Method using lignans for inhibiting overactivity of phagocytes or lymphocytes in an individual, and

therapeutic use. Ahotupa, Markku; **Eriksson, John**; **Kangas, Lauri**; Unkila, Mikko; **Komi, Janne**; **Perala, Merja**; **Korte, Helena** (Finland). U.S. Pat. Appl. Publ. US 2003100514 A1 20030529, 10 pp. (English). CODEN: USXXCO. APPLICATION: US 2001-991971 20011126.

AB The invention provides a method for inhibiting the overactivity of phagocytes or lymphocytes in an individual by administering to the individual an effective amount of a lignan, wherein (i) the phagocytes are neutrophils and the lignan is **hydroxymatairesinol** or matairesinol or mixts. thereof; or (ii) the phagocytes are cells of myeloid origin and the lignan is enterolactone or **hydroxymatairesinol** or mixts. thereof; or (iii) the lymphocytes are T-lymphocytes and the lignan is **hydroxymatairesinol**, matairesinol or enterolactone or mixts. thereof. The invention also provides a method for treating or preventing an acute ischemia-reperfusion injury or a chronic condition, caused by overactivity of phagocytes or lymphocytes in an individual, the method comprising decreasing the activity of phagocytes in an individual by administering to the individual an effective amount of a lignan.

L10 ANSWER 7 OF 11 BIOSIS COPYRIGHT (c) 2004 The Thomson Corporation. on STN

2002:583081 Document No.: PREV200200583081. USE OF **HYDROXYMATAIRESINOL** FOR PREVENTION OF CANCERS, NON-CANCER, HORMONE DEPENDENT DISEASES AND CARDIOVASCULAR DISEASES BY **HYDROXYMATAIRESINOL**, AND A PHARMACEUTICAL PREPARATION, FOOD ADDITIVE AND FOOD PRODUCT COMPRISING **HYDROXYMATAIRESINOL.** Ahotupa, Markku [Inventor, Reprint author]; Eckerman, Chester [Inventor]; **Kangas, Lauri** [Inventor]; Makela, Sari [Inventor]; Saarinen, Niina [Inventor]; Santti, Risto [Inventor]; Warri, Anni [Inventor]. Turku, Finland. ASSIGNEE: Hormos Nutraceutical Oy Ltd., Turku, Finland. Patent Info.: US 6451849 September 17, 2002. Official Gazette of the United States Patent and Trademark Office Patents, (Sep. 17, 2002) Vol. 1262, No. 3. http://www.uspto.gov/web/menu/patdata.html. e-file.
CODEN: OGUPE7. ISSN: 0098-1133. Language: English.

AB This invention relates to methods for prevention of cancers, certain non-cancer, hormone dependent diseases and/or cardiovascular diseases in a person, based on administering of **hydroxymatairesinol** to said person. The invention also concerns a method for increasing the level of enterolactone or another metabolite of **hydroxymatairesinol** in a person's serum thereby causing prevention of a cancer or a certain non-cancer, hormone dependent disease in a person, based on administering of **hydroxymatairesinol** to said person. Furthermore, this invention relates to pharmaceutical preparations, food additives and food products comprising **hydroxymatairesinol.**

L10 ANSWER 8 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN

2002:392225 Document No. 136:380145 Prevention of cancers, non-cancerous hormone-dependent diseases, and cardiovascular diseases by use of **hydroxymatairesinol**, and a pharmaceutical preparation, food additive and food product comprising **hydroxymatairesinol.** Ahotupa, Markku; Eckerman, Christer; **Kangas, Lauri**; Makela, Sari; Saarinen, Niina; Santti, Risto; Warri, Anni (Hormos Nutraceutical oy Ltd., Finland). U.S. Pat. Appl. Publ. US 2002061854 A1 20020523, 15 pp., Cont.-in-part of U.S. Ser. No. 829,944. (English). CODEN: USXXCO. APPLICATION: US 2001-972850 20011010. PRIORITY: US 1999-281094 19990330; US 2001-829944 20010411.

AB The invention discloses methods for prevention of cancers, certain non-cancerous, hormone-dependent diseases, and/or cardiovascular diseases in a person, based on the administration of **hydroxymatairesinol.** The invention also discloses a method for increasing the level of enterolactone or another metabolite of **hydroxymatairesinol** in a person's serum, thereby causing prevention of a cancer or a certain non-cancerous, hormone-dependent disease in a person, based on administration of **hydroxymatairesinol.** Furthermore, the

invention discloses pharmaceutical prepns., food additives, and food products comprising **hydroxymatairesinol.**

L10 ANSWER 9 OF 11 MEDLINE on STN DUPLICATE 2
2003059990. PubMed ID: 12570335. Antioxidant and antitumor effects of **hydroxymatairesinol** (HM-3000, HMR), a lignan isolated from the knots of spruce. **Kangas Lauri**; Saarinen Niina; Mutanen Marja; Ahotupa Markku; Hirsinummi Riikka; Unkila Mikko; **Perala Merja**; Soininen Pasi; Laatikainen Reino; **Korte Helena**; Santti Risto. (Hormos Nutraceutical Ltd, Turku, Finland.) European journal of cancer prevention : official journal of the European Cancer Prevention Organisation (ECP), (2002 Aug) 11 Suppl 2 S48-57. Journal code: 9300837. ISSN: 0959-8278. Pub. country: England: United Kingdom. Language: English.

AB The antioxidant properties of **hydroxymatairesinol** (HM-3000) were studied in vitro in lipid peroxidation, superoxide and peroxyl radical scavenging, and LDL-oxidation models in comparison with the known synthetic antioxidants Trolox (a water-soluble vitamin E derivative), butylated hydroxyanisol (BHA) and butylated hydroxytoluene (BHT). On a molar basis HM-3000 was a more effective antioxidant than Trolox in all assays and more effective than BHT or BHA in lipid peroxidation and superoxide scavenging test. The in vivo antioxidative effect (evaluated as the weight gain of C57BL/6J mice fed an alpha-tocopherol-deficient diet) of HM-3000 (500 mg/kg per day) was comparable to that of DL-alpha-tocopherol (766 mg/kg per day). The antitumor activity of HM-3000 was studied in dimethylbenz[a]anthracene (DMBA)-induced rat mammary cancer. HM-3000 had a statistically significant inhibitory effect on tumor growth. Prevention of tumor formation was also evaluated in the Apc(Min) mice model, which develops intestinal polyps spontaneously. HM-3000 was given in diet at 30 mg/kg per day and decreased the formation of polyps and prevented beta-catenin accumulation into the nucleus, the pathophysiological hallmark of polyp formation in this mouse model. In short-term toxicity studies (up to 28 days) HM-3000 was essentially non-toxic when given p.o. to rats and dogs (daily doses up to 2000 and 665 mg/kg, respectively); HM-3000 was shown to be well absorbed (> 50% of the dose) and rapidly eliminated. In human studies HM-3000 has been given in single doses up to 1350 mg to healthy male volunteers without treatment-related adverse events. Rapid absorption from the gastrointestinal tract and partial metabolism to enterolactone in humans was demonstrated. In summary, HM-3000 is a safe, novel enterolactone precursor lignan with antioxidant and antitumor properties.

L10 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2004 ACS on STN
2000:725669 Document No. 133:286508 **Hydroxymatairesinol** preparations in cancer prevention. Ahotupa, Markku; Eckerman, Christer; **Kangas, Lauri**; Makela, Sari; Saarinen, Niina; Santti, Risto; Warri, Anni (Hormos Nutraceutical Oy Ltd., Finland). PCT Int. Appl. WO 2000059946 A1 20001012, 43 pp. DESIGNATED STATES: W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (English). CODEN: PIXXD2. APPLICATION: WO 2000-FI181 20000309. PRIORITY: US 1999-281094 19990330.

AB This invention relates to methods for prevention of cancers, certain non-cancer, hormone dependent diseases and/or cardiovascular diseases in a person, based on administering of **hydroxymatairesinol** to said person. The invention also concerns a method for increasing the level of enterolactone or another metabolite of **hydroxymatairesinol** in a person's serum thereby causing prevention of a cancer or a certain non-cancer, hormone dependent disease in a person, based on administering of **hydroxymatairesinol** to said person. Furthermore, this invention relates to pharmaceutical prepns., food additives and food products comprising **hydroxymatairesinol.**

L10 ANSWER 11 OF 11 MEDLINE on STN DUPLICATE 3
2001103469. PubMed ID: 10890032. **Hydroxymatairesinol**, a novel enterolactone precursor with antitumor properties from coniferous tree (Picea abies). Saarinen N M; Warri A; Makela S I; Eckerman C; Reunanen M; Ahotupa M; Salmi S M; Franke A A; **Kangas L**; Santti R. (Department of Anatomy, University of Turku, Finland.) Nutrition and cancer, (2000) 36 (2) 207-16. Journal code: 7905040. ISSN: 0163-5581. Pub. country: United States. Language: English.

AB The potential for the extraction of the plant lignan **hydroxymatairesinol** (HMR) in large scale from Norway spruce (Picea abies) has given us the opportunity to study the metabolism and biological actions of HMR in animals. HMR, the most abundant single component of spruce lignans, was metabolized to enterolactone (ENL) as the major metabolite in rats after oral administration. The amounts of urinary ENL increased with the dose of HMR (from 3 to 50 mg/kg), and only minor amounts of unmetabolized HMR isomers and other lignans were found in urine. HMR (15 mg/kg body wt po) given for 51 days decreased the number of growing tumors and increased the proportion of regressing and stabilized tumors in the rat dimethylbenz[a]anthracene-induced mammary tumor model. HMR (50 mg/kg body wt) did not exert estrogenic or antiestrogenic activity in the uterine growth test in immature rats. HMR also showed no antiandrogenic responses in the growth of accessory sex glands in adult male rats. Neither ENL nor enterodiol showed estrogenic or antiestrogenic activity via a classical alpha- or beta-type estrogen receptor-mediated pathway in vitro at < 1.0 microM. HMR was an effective antioxidant in vitro.

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COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	209.30	209.51

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
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